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OBITUARY

JAMES CLYDE SARGENT

James Clyde Sargent was born on October 3, 1892 in Piqua, Ohio. He died on October 7, 1954. He was stricken with a posterior coronary occlusion while he was attending the annual meeting of the North Central Section of the American Urological Association in Detroit, Michigan.

Jim's grandfather, father and two uncles were Baptist ministers. His excellent poise and diction must have stemmed from this ancestry. His first ambition was to become an electrical engineer. The family moved to Columbus, Ohio to be near such a school. He was working for an electric company to make money for his education when he received a high voltage shock. The doctors discovered, at that time, pulmonary tuberculosis. As soon as possible, Jim procured a hotel job on Mackinac Island where he could have the benefit of good food and outdoors. The pulmonary condition soon healed. However, he became a sort of male nurse in the small hospital on Mackinac Island and learned to give anesthetics. This experience led to his desire to go to medical college. His parents objected strenuously. However, after 6 weeks of concentrated study and excellent grades, the family agreed to help him. So, he graduated from the Ohio Medical College—now the medical school of Ohio State University—in 1915.

He was in medical school in 1913 when the Ohio flood occurred. He and his roommate manned a flat-bottom boat to rescue people who had been caught in the flood. They rescued a family of five from the top of a house, which was swept by rapid torrents of the river. The Carnegie medal and $1000 were given to Jim and his roommate for this heroic act.

He served his internship in the Minneapolis City Hospital during 1915 and 1916. He did postgraduate study in the James Buchanan Brady Urological Institute, Johns Hopkins Hospital during 1916 and 1917. He came to Milwaukee, Wisconsin in 1917 and limited his medical practice to urology. His dynamic personality brought him many appointments and accomplishments. He became the clinical professor and director of the department of urology of Marquette University School of Medicine. He was on the urological staffs of St. Joseph, Evangelical Deaconess, Milwaukee County General, Milwaukee County Emergency and Johnston Emergency Hospitals. He was the urological consultant of the United States Naval Hospital, Great Lakes, Illinois, to the Surgeon General of the United States Navy and the United States Veterans Administration Hospital, Wood, Wisconsin. He served as a Captain of the Medical Corps of the United States Naval Reserves from 1942 to 1945.

Doctor Sargent's medical leadership began in 1931 when he was president of the Medical Society of Milwaukee County. He devoted his term of office to establishing the first medical society-sponsored prepayment plan for hospital care in this country. His opponents thought he was a crackpot, but time has shown that he was several years ahead of the procession. He was president of the Wisconsin Medical Society in 1937 and of the North Central Section of the

American Urological Association in 1948. He was a member of Phi Gamma Delta, Alpha Kappa Kappa and Shriners, Rotary Club and American Legion.

Doctor Sargent wrote many splendid articles on urological subjects. He was particularly interested in trauma of the urinary tract. One of his last literary efforts is the chapter on Injuries of the Genito-Urinary Tract in Dr. Meredith Campbell's three volumes. His close association with Federal Civil Defense authorities led him to write many articles in which he attempted to shock the public out of its apathy about civil defense.

He was a delegate of the American Medical Association and gained national recognition on the National Security Resources Board, Health Resources Advisory Commission and the National Advisory Commission on the selection of doctors, dentists and allied specialists of the Selective Service System. His numerous trips to Washington, D. C. were most time-consuming, but he did much to deter the proponents of socialized medicine. It was my privilege to serve on the latter committee several years with him and I was much impressed with his general and parliamentary knowledge.

Doctor Sargent was united in marriage with Mary Genevieve Cook on January 3, 1917. She survives him. They were blessed with three children. His son, James Wellington Sargent, is a urologist and has continued his father's practice. One daughter, Mary Genevieve, is married to Andrew Galbraith Miller and lives in Pewaukee, Wisconsin. The other daughter, Suzanne, is married to Robert Llewellyn Warnock and lives in Indio, California. Jim built a summer home on Lake Michigan near Cedar Grove where he could be with his family and his eight grandchildren. The latter will miss the grandfather because he spent much time in teaching them rhymes and songs around the beach fire. Jim loved to hunt. Each October he would build a blind on the shore near his lake home to shoot at migrating ducks. He was never too tired to tramp the fields for pheasants.

His was a full and interesting life. In 1951, he received the Alumni Achievement award of the Ohio State University College of Medicine, at the dedication of its new health center. He was, however, very proud when he was elected to membership in the American Association of Genito-Urinary Surgeons in 1951, and considered this one of his greatest honors.

William J. Baker, M.D.

BARRINGER MEDAL

Dr. Fletcher H. Colby: On March 14, 1953 this society lost one of its most cherished and loyal members, Dr. Benjamin S. Barringer. To perpetuate his memory and to stimulate progressive work in our specialty, our former president's family instituted the Barringer Medal. All scientists, regardless of race, color, sex or creed are eligible for this medal whether they are engaged in the practice of urology, any other medical specialty, or any study related to medicine. The medal is to be presented every other year at the annual meeting of this Association. A committee will choose the recipient on the basis of the proved value of his or her work to clinical urology, but will especially favor contributions promoting the treatment of tumors of the genitourinary organs, since this was Dr. Barringer's greatest interest.

Dr. Charles Huggins, you have been selected from many to be the first to receive the Barringer Medal. To me, this is most suitable. We are all aware of the many important contributions you have made to Medicine and to our specialty.

When Dr. Huggins was called to the University of Chicago in 1926 as an instructor in surgery he was told that one requisite was that he was to do research work. Probably his first step in this direction was to operate upon a dog. I doubt if ever before had he investigated the bladder of a dog, but being of an inquisitive nature he pried into this recess carefully. The result was a beautifully written and illustrated paper on the transplantation of bladder mucous membrane to the fascia of the abdominal wall with the production of true bone. As a result of this work, the physiological chemist was able accurately to date bone formation for the first time.

Since 1936 Dr. Huggins has been professor of surgery and chairman of the Department of Urology and has devoted much of his time to research as director of the laboratory. He has received many honors and awards including the honorary degree of Master of Science from Acadia University, Master of Science from Yale University and Doctor of Science from Washington University in St. Louis. In 1936 and 1940 he received gold medals from the American Medical Association for his scientific exhibits. In 1943 he was given the Charles L. Mayer award for cancer research by the National Academy of Sciences. In 1948 he received the Francis Amory award. These are only some of the things that have distinguished him. One of your best citations came from your former teacher of physiological chemistry in these words, "Charlie Huggins never became self conscious and never considered any limitations."

Many are the contributions you have made, Charles Huggins, and many are the well-deserved honors you have received. Your hours of labor have been long.

Charles Huggins, the American Association of Genito-Urinary Surgeons is honored in presenting to you the Barringer Medal.

Response by Dr. Huggins: It may be that at times I have been able to maintain some composure but I am not sure that this is one of those times. It is a moment of emotion. My associates and I are gratified by the recognition of our

work by this distinguished Association formed of many of the outstanding urological surgeons both of our country and abroad. We find it particularly pleasing that this beautiful medal has inscribed upon it the name of a famous urologist, Benjamin Stockwell Barringer. Dr. Barringer was the first to devote himself exclusively to the recognition and treatment of tumors of the urinary tract and in this field he made two important contributions. First, he showed that it was possible, by the judicious and skillful implantation of radium and its isotope radon, to bring about cures of cancer of the bladder. Hundreds of patients were cured by him through this instrumentality. Secondly, Dr. Barringer found that cancer of the prostate could not be controlled by the local interstitial application of radioactivity—a lesson which was forgotten and has needed to be relearned—and he abandoned this method soon after the introduction of the antiandrogenic treatment of prostatic cancer.

It is not generally remembered that Barringer and Helen Woodard, independently and contemporaneously with A. B. Gutman and E. B. Gutman in 1938, showed that acid phosphatase is sometimes increased in the blood of patients with cancer of the prostate which has become disseminated. This discovery was to be utilized by lesser men subsequently in proving that testosterone activates this cancer whereas it is inactivated by orchiectomy and estrogenic substances.

Dr. Barringer trained a number of pupils during his long and active career, many of whom became accomplished yachtsmen and I suspect that their surgical training was supplemented by an informal course in sailing. He participated actively in meetings of medical societies where he contributed generously of his knowledge for the benefit of man.

Long may the Association honor the memory of Benjamin Stockwell Barringer, rock of integrity, pillar of honesty, white flame in the advancement of knowledge, and friend!

Our work was done by more than a hundred young men and women, mostly medical students and residents in training, and being infinitely lazy I am indebted to them. Of course, not a hundred at any one time but merely two or three—it is not well to have many doves flitting in and out of the workshop when serious activity is taking place. In addition to their massive contribution to our program, I thoroughly enjoyed the vast amount of conversation which was necessary in this work. It was done in a university setting. A university is not a library but a place where there is much talk about intellectual matters and if the conversation is inspired a great university ensues.

Much of the work of my young co-workers had to do with the effects of steroids on tumors of man. After we had proven that cancer of the prostate is often dependent on hormones this new concept was verified by a number of workers and hormonal measures of control have become standard practice throughout the world. A subsequent development was the treatment of leukemia and allied diseases with cortisone by an intelligent group of workers at Memorial Hospital led by O. H. Pearson. In this disease brilliant control is frequently achieved but with agonizingly brief remissions.

For the last 4 years we have been working actively on cancer of the breast—a problem of great nobility since it is the commonest tumor of the race. Mammary cancer has its pattern of great tragedy. Over and over again the consultant is faced by the patient with this disseminated tumor who is usually calm and resigned to suffering and death which she commonly accepts with equanimity. And with her is the husband, poor soul—he with the pale face and the rapid pulse and the trembling hands—at his wits' ends but he cannot let her go.

Well, gentlemen, at times something can be done for these women after all else has failed, by adrenalectomy. The suprarenal glands, in common with the ovaries, make sex hormones which activate dependent mammary cancers and these regress when the hormonal support is withdrawn by surgical means. It is our belief that, after age 54 in the human female, adrenalectomy alone will usually give adequate steroid withdrawal.

Why should adrenalectomy for mammary cancer be of interest to the urological surgeon? Simply because the easiest surgical approach to the adrenal is through the loin and the urologist, among the surgeons, is most experienced in this type of surgery. Of course, specialization is based on therapeutic competence, not on an organic basis and this brings adrenal surgery—for whatever reason—in the urological field.

Well, then, we see that in the short space of 14 years 3 grave cancers have been attacked, with more or less success—generally less, by hormonal means. Is it reasonable to predict that all possible therapy, with all conceivable steroids has been employed for every susceptible cancer and that the list is now complete?

And now, reiterating our thanks, I shall hurry home to have this handsome medal divided into more than a hundred pieces so that the rightful recipients can have their shares.

THE EFFECT OF CORTISONE ON THE SPERMATOGENIC FUNCTION OF THE HUMAN TESTES

JAMES H. McDONALD AND NORRIS J. HECKEL

From the Department of Urology of The Presbyterian Hospital of Chicago in affiliation with the University of Illinois College of Medicine, Chicago, Ill.

Recent experimental evidence has shown that cortisone may influence spermatogenesis in the laboratory animal.

Cavallero, Rossi, and Borasi[1] found diminished testicular weight and a depression of spermatogenesis in rats treated with 1 mg. of cortisone acetate daily for 70 days followed by 5 mg. daily for 20 days. Antopol[2] found a decrease in testicular size and varying degrees of arrest of spermatogenesis in the mouse after the administration of cortisone.

Ingle,[3] and Winter, Silber, and Stoerk[4] found that 5 mg. and 3 mg. respectively of cortisone acetate daily did not produce a significant decrease in weight of the adult rat testes. Gaunt,[5] as well as Finerty,[6] found a relative, but not actual, increase in the weight of the rat testes after cortisone was given. They explain this as due to the lack of effect of the growth-inhibiting property of cortisone on the testes.

Sprague[7] has suggested that cortisone might have weak androgenic effects. He also feels that cortisone may cause a decrease in human libido.

Wilkins and Cara[8] used cortisone in the treatment of male children with congenital adrenal hyperplasia. They made a study of the testicular biopsies before and after therapy and noted that in those children above 7 years of age (bone age 13–14 years) there was an increase in spermatogenesis corresponding to that of the young adult. In the age group of 5 to 7 years (bone age 11 years), treatment caused a general maturation with some spermatid formation, and below 5 years of age (bone age 9–10½ years) little histological change was seen.

To determine the effect of cortisone upon spermatogenesis in adult man, a correlative study of seminal fluids and testicular biopsies has been carried out in a group of patients given this drug.

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MATERIALS AND METHODS

Four patients were selected from a large group with arthritic disease specifically requiring cortisone therapy. Because of the high incidence of oligospermia in this group, 7 patients with normal spermatozoa counts were selected from the urological department of a free clinic.

A complete general history and a specific sexual history were obtained. Each man had a complete physical examination. Special attention was given to the examination of the external genitalia and prostate. Routine laboratory studies were done on each patient as well as special urological examinations when indicated.

These men were in general good health except for minimal urological disease and the disease requiring treatment with cortisone. The age of the patients ranged from 33 to 74 years. The examination of the genitalia revealed the testes, in most instances, to be normal and the prostate to be enlarged by benign hyperplasia in three of the patients.

Semen specimens were obtained by masturbation in the laboratory after abstinence from sexual intercourse for at least 5 days. The specimens were collected in clean, wide-mouth glass containers. The analyses included observations on the volume, motility, numbers of spermatozoa (reported in millions per cubic centimeter), pH, and morphology. A minimum of three specimens were examined before treatment and at one to six week intervals during treatment.

Testicular biopsies were performed prior to treatment and during, or at the end of, therapy. The biopsies were unilateral and in the same organ when more than one biopsy was secured. The testicular tissue was obtained by incision and the material immediately fixed in freshly prepared Bouin's solution. The sections were stained with hematoxylin and eosin and Masson's trichrome technique.

The eleven men were given 75 mg. of oral cortisone* daily in three divided doses. In addition, 30 gr. potassium chloride were administered daily.

RESULTS

Seventy-five milligrams of cortisone were given daily over periods varying from 23 to 334 days. After 2 weeks' treatment, the cortisone was stopped in one patient because of hemorrhage in an unsuspected duodenal ulcer. No other complication of treatment was encountered.

Seminal fluid specimens prior to treatment revealed 2 of the patients to be oligospermic. One patient was unable to produce semen specimens.

The numbers of spermatozoa in the 10 patients securing specimens revealed the variabilities during treatment to be not significantly different from the variation before or after the drug was given. Similarly, there was no significant alteration in the sperm motility or normal morphology during treatment as compared to the specimens secured before and after treatment.

Testicular biopsy was performed on the 11 patients prior to therapy. Biopsies were also done on 6 patients during or at the end of the cortisone treatment. In

* The cortisone acetate (cortone) was supplied for this study through the generosity of Merck & Co., Inc., Rahway, N. J.

these 6 patients, histological examination of the pretreatment and post-treatment biopsies revealed no significant change.

No history of alteration of libido could be elicited from the ten potent patients.

CONCLUSIONS

Cortisone in amounts of 75 mg. daily does not alter the spermatogenic function of the adult human testes.

There is no significant difference between pretreatment spermatozoa counts and those obtained during and after treatment with cortisone.

There is no alteration in spermatozoa motility or morphology produced by the treatment with cortisone.

In 6 patients there was no significant change in the germinal cell elements as evidenced by histological examination of testicular biopsies before and after cortisone therapy.

UNDESCENDED TESTES: REPORT OF 153 CASES WITH EVALUATION OF CLINICAL FINDINGS, TREATMENT, AND RESULTS ON FOLLOWUP UP TO THIRTY-THREE YEARS

JOHN R. HAND

In this series orchiopexy was deferred until puberty unless complications demanded earlier intervention. Such a course resulted in placement of some testes before puberty. It allowed others to descend spontaneously. It encouraged trial of chorionic gonadotrophin to aid descent of still others, with completion of descent in a small number.

A followup of many years in the majority of the patients permitted long range consideration of the results. The evaluation was aimed in two directions: 1) the cosmetic status as evidenced by the position, size, and consistency of the testes after they had reached the scrotum by delayed descent or by orchiopexy; 2) the physiologic status of these testes.

The study calls attention to the significant number of testes that were retained after puberty, and emphasizes the damage that ensued. It also points up the variation in the behavior of individual testes, even in the same patient.

DESCRIPTION OF MATERIAL

The series includes 153 consecutive patients seen by the physicians in The Portland Clinic from January 1, 1922 to April 1, 1955. Fifty-one had bilateral and 102 had unilateral retention, making a total of 204 testes in the series. Management of 20 testes was carried out elsewhere.

All but 3 patients were traced. Of these, 2 had bilateral and 1 unilateral retention. In discussing some clinical features all 153 patients are included; in other instances only those traced are considered.

The patients were grouped according to similarity in the fate of one or both testes (table 1). Of 3 in the category "under observation," 2 with bilateral retention have perineal hypospadias which is being corrected. A fourth patient with 1 testis under observation had spontaneous descent of the mate and is listed under the latter category.

This grouping was followed, first, to determine if there was a difference in the clinical course of bilateral and unilateral undescended testes; second, to evaluate the response to hormone therapy in the respective groups; and, third, to compare fertility performance following bilateral delayed descent with that after surgical management here and elsewhere.

CLINICAL FINDINGS

Age. Table 2 shows the age at which the testes of the respective patients descended to the scrotum or were managed by some operative procedure. When both testes did not reach the scrotum at the same time, the age at which the first completed its descent is shown in this and in other pertinent analyses. In the majority of patients this corresponded to the age on admission. The patients

TABLE 1. *Fate of 204 undescended testes in 153 patients*

Fate of Testes Here and Elsewhere	Bilateral Retention		Unilateral Retention
	No. pts.	No. testes	No. pts. and testes
Delayed descent	13	26	8
1 side delayed descent, 1 side other fate*	10	20	—
1 side orchiopexy, 1 side other operation†	4	8	—
Orchiopexy‡	18	36	40
Primary orchiectomy	—	—	30
Explored, not found	1	2	3
Epididymal remnants removed	—	—	4
Testes replaced in abdomen	1	2	—
Under observation	2	4	1
Treatment not followed as advised	—	—	15
Not traced	2	4	1
Total	51	102	102

* Orchiopexy, 6 testes; orchiectomy, 1; exploration, 1; epididymal remnant removed, 1, under observation, 1.

† Primary orchiectomy, 3 testes; epididymal remnant removed, 1.

‡ Secondary orchiectomy, 4 testes—1 patient with bilateral and 3 with unilateral retention.

under observation and those who have not had treatment as advised are listed according to their ages on admission.

Variations in the limits of puberty make division into arbitrary age groups difficult. Indeed, 2 patients in the series at age 9 showed pubic hair, which is generally regarded as a criterion for the beginning of puberty. Nevertheless, because the others did not mature until later, patients through age 9 were designated as "prepuberal"; those from 10 through 17 years as "puberal"; and those 18 years and over as "adult." The youngest patient was 2, the oldest 73.

In the bilateral group there were about the same number of prepuberal and puberal patients, whereas only 8 were adults. In the unilateral group the number of patients increased in each successively older age division, 52 being adults. The wide difference between 8 adults in the first group and 52 in the second emphasizes the lack of concern the patient with unilateral retention has regarding his abnormality, particularly when it has not impaired his potency or fertility

TABLE 2. *Ages of 153 patients with undescended testes*

Age Treatment Was Done or Advised	Total Patients		Bilateral Retention		Unilateral Retention	
	No.	%	No. pts.	%	No. pts.	%
Prepuberal 1 through 9	30	19.61	19	37.25	11	10.78
Puberal 10 through 17	63	41.18	24	47.06	39	38.24
Adult 18 and over	60	39.21	8	15.6	52	50.98
Total	153		51		102	

and has not given rise to psychic trauma. Neglected placement of the testes past puberty in these patients led to orchiectomy.

Side of involvement. Of the 204 testes, 115 were on the right and 89 on the left side. The tendency for the right testis to lag has been mentioned by most writers. Meyer attributed the earlier descent of the left testis to the pressure of the sigmoid which is greater than that exerted by the cecum.

Position of testes. It is not always possible to determine the position of the testes by palpation. This may be due to agenesis or to arrest within the abdomen. Often an unusually small canalicular testis eludes detection. An associated hernial sac and obesity may contribute to the difficulty of palpation.

Of the 204 testes, the position of 8 could not be ascertained in patients operated on elsewhere prior to admission. Fifty-two testes could not be palpated on examination here. Of these, 3 were in patients not traced and 6 in patients not treated. Eleven subsequently descended spontaneously, either from the abdomen or the canal. Operation disclosed gonadal agenesis in 11 instances; it also showed arrest of 9 testes in the abdomen and 11 testes in the canal. And autopsy revealed 1 testis in the superficial inguinal pouch.

In the remaining 144 testes the positions on palpation were: canal, 62; external ring, 61; ectopic, 21. Adding to these the 20 testes located at operation and the 1 testis found at autopsy, the levels of arrest of 165 testes are known, and these are: abdomen, 9; canal, 73; external ring, 61; ectopic position, 22. Of the 22 testes, 2 proved to be in the femoral region, 2 in the pubopenile area and 18 in the superficial inguinal pouch.

Among the bilaterally undescended testes the largest number were arrested at the external ring, 38 of 61. The unilateral undescended testes were most often arrested in the canal, 42 of 73 (table 7).

Size of testes. The size of the testes at the initial examination was recorded in 103 instances. Of these, 86 were smaller than normal and 3 were large because of tumor (a fourth testicular tumor was intra-abdominal).

It is probably not generally realized that a considerable number of newborn infants exhibit disproportion in the size of their two testes. Recently on examining an infant in the maternity ward of St. Vincent's Hospital, I observed that one testis was about twice the size of its mate. Because of this I carefully examined the next 40 boys born. In 27 both testes were approximately the same size; in 13 one was larger than the other, the degree of disparity varying considerably from infant to infant.

Retractile testes. As used here, "retractile" means testes that are mobile. That is, they retract either after temporary scrotal residence (as revealed by the history and repeated observation) or when the fingers manipulating them toward the scrotum are withdrawn.

Of the 153 patients, 13 had 19 retractile testes. Three were in patients with unilateral retention. The other 16 were in 10 patients with bilateral retention, 4 of whom had a retractile testis on one side and 6 of whom had retractile testes on both sides. Retractability was established as follows:

Eight testes could be manipulated to the top of the scrotum. In each instance there was no scrotal development on the involved side.

Three testes were observed at different levels during repeated examinations. All 3 finally withdrew to the canal, including 1 that had been in the scrotum temporarily.

Eight testes in 6 patients were retractile by history. Three had had temporary scrotal residence. One of the 3 became trapped in the superficial inguinal pouch. The other 2, in 1 patient, were not palpable after they ascended but were felt at the external ring following hormone administration.

Of the 19 retractile testes, 13 subsequently descended to the scrotum spontaneously, 1 having had previous temporary scrotal residence. In 1 patient the testis descended at age 21, at which time it was atrophied; the others descended by age 12. The other 6 retractile testes were brought down by orchiopexy, all by age 17. Of these, 4 were associated with hernias, 1 was arrested in the superficial inguinal pouch, 1 was brought down elsewhere but had not been associated with a hernia on previous examination here. Three of the 6 had had previous temporary residence in the scrotum (2 with hernias, 1 arrested in the superficial inguinal pouch).

The size on initial examination was recorded for 9 of the retractile testes. Six were small and 3 normal.

Hereditary tendency. It seems more than coincidental that a tendency to undescended testes was exhibited by members of the families of 14 patients. The abnormality occurred in an uncle of 1 patient, in brothers of 5, in fathers of 2, and in 9 sons of 6 patients. Of the last, 2 patients had 1 son each, and each son had retention; the third patient had 2 sons, each of whom had incomplete descent; the fourth patient had 3 sons, 1 of whom had an undescended testis; the fifth patient had 4 sons, 1 of whom had an undescended testis; the sixth patient had 5 sons, 3 of whom, or every other one, had an undescended testis—in 1 boy the testis descended spontaneously, in 1 it came down in response to hormones, in 1 it was brought down by orchiopexy.

The mother of still another patient had agenesis of 1 ovary. Thus, a tendency to abnormality of the testes or ovary was noted in members of the families of 15 patients, or 9.8 per cent of the 153 patients in the series. Of the 15 patients, 11 had bilateral retention, or 1 in every 5 of the 51 patients in the bilateral group. Four had unilateral retention, or 1 in every 26 of the 102 patients in the unilateral group.

Evidence of such inherent tendencies was noted by Bishop, Brosius, Coley, Johnson, McCutcheon, Wangensteen, and others.

Associated abnormalities. Notes of mental retardation were made in the histories of 8 patients, one of whom is now in an institution. Two additional patients had schizophrenia and a third had involutional melancholia. Two of the 3 committed suicide.

Two additional patients had grand mal epilepsy. Still another had narcolepsy.

Seven boys were obese. Eight patients (2 puberal boys and 6 adults) exhibited eunuchoid characteristics. Six patients had gynecomastia which was bilateral in 2.

Two boys had perineal hypospadias. Both had bilateral retention. One had had an abdominal exploration prior to admission and no female genital organs were

found. Johnson noted hypospadias in 2 of 544 boys with undescended testes. Hooks stressed the importance of differentiating between retention and dimorphism in these patients, stating that while fertility is not a problem in those with the latter condition an error in diagnosis may interfere with their sociologic adjustment.

Two boys were deaf. Both had bilateral retention. One boy with unilateral retention had congenital dislocation of the hips.

TREATMENT

No treatment. Fourteen patients with involvement of 26 testes (12 with bilateral and 2 with unilateral retention) had neither hormones nor operations. Twenty-two testes descended spontaneously, as follows (table 3):

Sixteen testes in 8 patients represent bilateral descent. Of these, 8 came down at the same age; 8 came down at different ages.

Four testes represent descent on one side in 4 patients with bilateral retention, the opposite side requiring operation.

Two testes represent descent in 2 patients with unilateral retention.

Hormone therapy. Injections of chorionic gonadotrophin were given to 47 patients, 22 with bilateral and 25 with unilateral retention. They had involvement of 69 testes.

The doses ranged from 1,625 to 50,000 international units. Only 4 patients received 36,000 or more.

The series is too small and the doses for the most part are not large enough by current standards to warrant conclusions. Also, in many instances the hormone was given prior to 1947, when more potent preparations became available and larger doses were being given. Nevertheless, the results bear review.

Descent was attributed to the treatment if the testes came down within a month after administration of the hormone. On this basis, 16 testes responded to the treatment (table 3). These were in 14 patients, 9 with bilateral and 5 with unilateral retention. Four were patients who had received the large doses of hormone. Of the 9 patients with bilateral retention, 2 had bilateral response, the other 7 had response on one side.

The youngest patient to receive chorionic gonadotrophin was 7 years old. The youngest to show response was 8 years old.

Not responding to hormone stimulation, but subsequently descending spontaneously at puberty were 6 testes of 4 patients, 3 of whom had bilateral retention. In 1 of the 3 both testes descended at the same age; in the second there was an interval of 3 years between descent of the 2 testes; in the third 1 testis had responded to hormone stimulation 2 years previously.

Chorionic gonadotrophin, in doses ranging from 5,000 to 6,000 units, was given to 6 of the 7 obese boys. The six boys had 9 clinically undescended testes. Of these, 4 responded to the hormone; 3 did not respond but subsequently descended spontaneously; 2 were not found on exploration. All 7 obese boys were given suitable dietary instructions. Two required thyroid extract.

Recapitulation of testes descending without operation (spontaneous descent). From

TABLE 3. *Performance of 95 testes in 61 patients: 26 in 14 patients having no hormones, 69 in 47 patients given hormones*

Fate of Testes	Total Testes		Bilateral Retention		Unilateral Retention		Age Testes Reached Scrotum without Operation		
			No. testes	No. retractile	No. testes	No. retractile	Prepuberal	Puberal	Adult
No hormones:									
Spontaneous descent		22	20	3 (15.0%)	2	—	6—2 at 7 4 at 9	14—3 at 10 1 at 11 5 at 12 2 at 13 1 at 14 2 at 15	2—1 at 18 1 at 21
Other fate: Orchiopexy, 1 Orchiectomy, 2 Agenesis, 1	4		4						
Hormone therapy:									
Immediate response		16	11	4 (36.36%)	5	1 (20.0%)	6—1 at 8 5 at 9	10—4 at 10 1 at 11 5 at 12	—
No responses: (53 testes)									
Descent later		6	5	4 (80.0%)	1	1 (100.0%)	1—at 9	5—at 12	
Other fate: Orchiopexy, 37 Orchiectomy, 2 Agenesis, 5 Observation, 2 No treatment, 1	47		28	1 —	19	—			
Total	51	44	68	12 (17.65%)	27	2 (7.41%)	15	27	2

TABLE 4. *Age at which 44 testes in 31 patients descended spontaneously—with and without hormone stimulation*

Explanation of Descent	No. Pts.	No. Testes	Age Testes Descended										
			Prepuberal			Puberal						Adult	
			7	8	9	10	11	12	13	14	15	18	21
Bilateral retention:													
Both same age	7	14	—	—	6	2	—	6	—	—	—	—	—
Each different age	6	12	1	—	1	2	—	4	2	—	1	1	—
One side only	10	10	—	1	3	—	1	2	—	1	1	—	1
Unilateral retention	8	8	1	—	—	3	1	3	—	—	—	—	—
Total	31	44	2	1	10	7	2	15	2	1	2	1	1
			13 (29.55%)			29 (65.91%)						2 (4.55%)	

the foregoing, and as noted by others,* it is evident that a significant number of testes descend spontaneously, that is, without the aid of hormones, whereas some reach the scrotum in response to hormone stimulation. Strictly, the latter do not "descend spontaneously." But since, like the first, they do not require operative placement they are considered in this category.

While testes that descend spontaneously after birth, even as late as puberty, are not regarded as typical undescended testes, they have been included here for the sake of completeness. First, they demonstrate that in a considerable number of patients deferment of operative intervention is justifiable. Second, their long residence outside the scrotum and their subsequent corrected position without the trauma incident to operative manipulation make evaluation of their status after reaching the scrotum a good yardstick for comparison with the status of testes brought down by orchiopexy.

Table 3 recapitulates the data pertaining to the 95 testes of the 61 patients who either had had no treatment or who had been given hormones. Since there were among them 34 with bilateral retention, the fate of both testes is shown.

There was, then, descent without operation in a total of 44 testes—in 31 patients, 23 of whom had bilateral and 8 of whom had unilateral retention. This represents 22.1 per cent of 199 testes in 49 patients with bilateral and 101 patients with unilateral retention who were traced. On the basis of these data, one can say the possibility of descent among patients with bilateral retention is 1 in 2, and among patients with unilateral retention it is 1 in 9.

Although 23 of the 31 patients had bilateral retention, bilateral descent occurred in only 13. In 7 of the 13 patients both testes came down together. In 6 there was a lapse of from 2 to 6 years between descent of the first and second testis, but in each patient, as previously stated, 1 testis was down by the age of 13. In 4 of the 6 patients the right testis lagged behind the left.

The relationship of age to descent and the side involved is shown in table 4. By the age of 12 all but 7 testes had reached the scrotum. Five more came down

* Bishop; Deming; Johnson; McCutcheon; Mimpriss; Rea; Smith (1954); Thompson, Beven, Heckel, McCarthy and Thompson. See list of references for place of publication.

TABLE 5. *Operations for 138 clinically undescended testes*

Procedure	Total Ops.	Side Involved		Age at Operation			Ops. Else.
		Bil.	Unil.	Prepub.	Puberal	Adult	
1 stage orchiopexy	59	32	27	15	33	11	8
2 stage orchiopexy	27	15	12	5	14	8	1
Secondary orchiectomy	4	1	3	—	—	4	1
Primary orchiectomy	35	5	30	—	3	32	7
Explored, not found	6	3	3	—	6	—	1
Remnants of epididymis or vas removed	5	1	4	—	—	5	—
Both testes put in abdomen, rings closed	2	2	—	2	—	—	2
Total	138	59	79	22	56	60	20

by the age of 15, leaving 2 that descended after puberty. The range in the age of descent was not so great among the 8 testes in the unilateral group as it was in the 26 testes in the bilateral group.

At the initial examination, 8 of the 44 testes were palpable in the canal and 22 at the external ring. Eleven could not be palpated and may have been either in the abdomen or in the canal. Three testes had descended before admission, and the levels of their arrest could not be determined. None was palpable in an ectopic position. None was associated with a hernia.

Operative correction. Shown in table 5 are the various operative procedures carried out here and elsewhere on 138 clinically undescended testes. The one-stage orchiopexies were done most often and are modifications of the procedures described by Bevan and by Cabot and Nesbit. The two-stage orchiopexies are those developed by Torek and by Keetley.

The majority of the operations, or 78, were done by the time of puberty. Of these, 67 were to place the testes, 34 being in patients with bilateral and 33 in patients with unilateral retention.

The patients with bilateral undescended testes required 59 operative procedures, whereas those with unilateral undescended testes had 79 operations. But 30 of the operations for unilateral retention were primary orchiectomies. Gonadal agenesis was more common among patients with unilateral retention, 7 as against 3 testes.

Secondary orchiectomies were done in 4 patients. In 1 the testis had been secured in the scrotum with a stitch at the time of herniorrhaphy at age 5. It retracted to the external ring. In the second patient the testis, which had not fused with the epididymis, was secured in the scrotum with a stitch at age 6. It retracted to the external ring and at operation elsewhere at age 21 it was atrophic —the opposite testis, brought down by orchiopexy elsewhere at age 15, showed the same anomaly of nonfusion. In the third patient torsion developed 7 days after orchiopexy and herniorrhaphy at age 30. The fourth patient had had the first stage of a Torek operation elsewhere at age 27. When he was seen here at

age 37, for another condition, the scrotum was still attached to the thigh and the testis was atrophied. It was removed 6 years later because of pain.

Complication of hernia. Occasionally the processus vaginalis is not demonstrated in an abdominal testis because it has either failed to develop or has fused completely. In the majority of patients it is formed, does not fuse completely and retains its communication with the abdomen. This creates a potential hernia. It is important to remember that while the potentiality of hernia is always present in the undescended testis, the hernia may not become of surgical significance.

Of the 49 patients with bilateral retention who were traced, 29 had 38 hernias requiring repair. All but 1 have been repaired. In addition, bilateral hernias were present in 1 patient not traced. Thus, of the total 51 patients with bilateral retention, 30, or 58.82 per cent, had a total of 40 hernias.

Among the 101 patients with unilateral retention who were traced, 49, or 48.51 per cent, had hernias requiring repair. Of these, 48 have been repaired; 1 has not in an adult who did not have treatment as advised.

The hernias repaired total 85. Sixty-eight were repaired here. Of these, 42 were diagnosed clinically; 25 were detected at the time of operation for correction of the retention.

Eighteen hernias were repaired elsewhere. When the patients were subsequently seen here, 7 testes were palpable at the external rings. One of the 7 testes, in a patient aged 10, was atrophied. His hernia repair was done at age 2; at age 4 the testis was brought down by orchiopexy. Two hernias, in 2 other patients, recurred. In still another patient both testes were replaced in the abdomen at age 8 and the external ring on each side was closed tight when bilateral hernias were repaired. On examination here 10 years later neither testis could be palpated.

Of the total 85 hernias repaired, 18 were in prepuberal boys, 34 in puberal boys and 33 in adults.

The levels of arrest of the testes associated with the hernias requiring repair were: abdomen, 6; canal, 46; external ring, 20; superficial inguinal pouch, 7. In 3 instances there was agenesis. In 3 patients operated on prior to admission the level of arrest could not be determined.

While none of the 44 testes that descended spontaneously had a concomitant hernia, hernias developed after the descent of 4. The intervals between descent and detection of the hernias were 6 months, 6 months, 2 years and 10 years, respectively.

Complication of torsion. A long mesentery in a loose sac and excessive contraction of the cremaster muscle predisposes to axial rotation of the cord, or torsion. Occurring more often with undescended than with scrotal testes, torsion often demands immediate operation. The ensuing infarction in the testis gives rise to severe pain which may lead to shock. It has been shown that if torsion persists for an hour or more the damage to the testis is irreparable. (Oettle and Harrison.)

Torsion developed in 3 patients in this series, and in each the pattern was

different. One patient, at age 12, had sudden pain which increased in severity and culminated in shock. Treatment consisted of relieving the torsion, repairing an associated hernia, and bringing the testis down by a one-stage orchiopexy. Recheck, at age 36, disclosed an atrophied testis. The second patient had had a hernia repair and one-stage orchiopexy at 30. Torsion developed 7 days later and necessitated orchiectomy. The third patient gave a history of recurring episodes of torsion. Orchiectomy was necessary at age 22 because of atrophy.

Complication of tumor. Seminoma was a third complication, being present in 4 testes. One of these was arrested in the right side of the abdomen, 1 in the right canal, 1 in the right superficial inguinal pouch, and 1 in the left superficial inguinal pouch. Since 22, or 9.81 per cent, of all the testes in the series were in ectopic positions, it is of interest that 2, or half, of the malignant testes were in such positions. Only the canalicular testis was associated with a demonstrable hernia.

The ages of the patients at orchiectomy were 26, 36, 37 and 37. Two had a normal scrotal testis on the opposite side. One had an atrophied scrotal testis. The fourth patient had a canalicular testis on the opposite side. Small and associated with a clinical hernia, this testis was brought down by orchiopexy.

In The Portland Clinic there were 26 additional patients who had cancer in 28 scrotal testes. On the basis of 32 malignant testes, the percentage of cancer in undescended testes in this clinic is 12.5 per cent; on the basis of 199 clinically retained testes in 150 patients traced, the percentage is 2.01. When the 44 testes that descended spontaneously are deducted, the percentage is slightly higher, being 2.76 per cent. Stray was of the opinion that malignancy may be associated with atrophy of the germinal epithelium.

Malignancy was not observed in testes brought down by orchiopexy nor in

TABLE 6. *Gross developmental anomalies of testicular structure*

Case	Age at Op.	Side Involved	Position Before Op.	Defect
1	12	1	Impalpable	No testis
2	12	1	Impalpable	No testis
3	14	1	Impalpable	No testis
4	15	2	Impalpable	No teste
5	25	1	Impalpable	No testis
6	18	1	Impalpable	No testis, rudimentary epididymis
7	22	1	Impalpable	No testis, rudimentary epididymis
8	32	1	Impalpable	No testis, rudimentary epididymis
9	38	1	Impalpable	No testis, rudimentary epididymis
10	34	1	Impalpable	No testis or epididymis, vas present
11	4 15	2	Canal	Hypoplastic testes, nonfusion with epididymides
12	73	1	Ext. ring	Hypoplastic testis and epididymis*
13	25	1	Ext. ring	Atrophied testis, focal atresia vas
14	12	1	Canal	Excessively short cord
15	15	1	Canal	Excessively short cord

* Contained ovarian as well as testicular elements.

those descending spontaneously. As indicated, the 4 malignant testes were retained until after puberty. Whether cancer would have developed if they had been placed in position before or at puberty is an interesting speculation. Gilbert and Hamilton stated that orchiopexy does not prevent latent malignancy. In their study they observed cancer in 77 testes after orchiopexy. Rusche noted malignancy after orchiopexy in 4 testes.

Associated defects. Gross developmental anomalies were noted in 17 testes of 15 patients, 4 with bilateral and 11 with unilateral clinical retention (table 6). Only 2 of the 4 patients had bilateral defects. Eleven defects represent agenesis. In 1 patient the tissue removed from the external ring contained ovarian as well as testicular elements.

The testes that were placed in position or removed had imperfections in the pathway to descent. These are described more fully in the discussion.

Relationship of position to fate of testes. Table 7 shows the relationship of the levels of arrest to the fate of the testes. It will be seen that the position was known for 85 testes in patients with unilateral retention and for 80 testes in patients with bilateral retention, a practically comparable number in each group.

Reaching the scrotum by orchiopexy or by spontaneous descent were 70.57 per cent of the 68 testes in the canal; 72.23 per cent of the 18 testes in ectopic positions; and 90.57 per cent of 52 testes at or below the external ring. Thus, the higher percentage of testes reaching the scrotum from the lower position can be attributed to the greater length of the cord structures.

It is frequently stated in the literature that mechanical factors are responsible for unilateral retention whereas failure of hormone response at birth prevents descent of bilaterally retained testes. This study indicates that such sharp distinctions cannot be made. Rather, the factors responsible for retention in one group are apparent also in the other.

For example, among the 85 unilateral undescended testes, shown in table 7, there were 7 testes that descended spontaneously, or 1 in 12. In these 7 testes

TABLE 7. *Relationship of position to fate of testes*

Known Level of Arrest	Number of Testes					Fate of Testes								
	Total	Side		Eliminated*	Included	Orchiopexy			Orchiectomy			Delayed descent		
		Bil.	Unil.			Bil.	Unil.	%	Bil.	Unil.	%	Bil.	Unil.	%
Abdomen	9	3	6	—	9	4	—	44.44	1	4	55.56	—	—	—
Canal	73	31	42	5	68	22	18	58.81†	3	17	29.41	6	2	11.76
External ring	61	38	23	8	53	18	8	49.06	—	5	9.43	17	5	41.51
Ectopic	22	8	14	4	18	4	9	72.23	1	4	27.78	—	—	—
Total	165	80	85	17	148	48	35	56.08	5	30	23.65	23	7	20.27

* Includes 6 testes (4 patients) expectant treatment; 9 in patients who have not had treatment as advised; 2 in patients not traced.

† 3 testes, 1 in patient with bilateral and 2 in patients with unilateral retention, subsequently removed.

there is no question of mechanical obstruction. Eliminating 11 testes with defects and the 7 that descended spontaneously leaves 67 testes mechanically obstructed. Among the 80 testes in the bilateral group, 23 descended spontaneously, or 1 in 4. This seems to support the premise that hormone failure at birth is a cause of bilateral retention. But when the 23 testes descending spontaneously and the 6 with defects are eliminated, there remain 51 mechanically obstructed.

EVALUATION OF MICROSECTIONS

Sections were available for review from 36 testes in the series. For comparison, sections were also obtained from 5 normally descended mates.

In table 8 an attempt has been made to show the degeneration in the retained testes as well as the extent to which spermatogenesis was recovered in the testes with scrotal residence after orchiopexy. The findings are grouped according to the time the tissue was obtained.

1. *Biopsy at orchiopexy.* Included here are sections of 6 testes. In all the basement membrane and the tunica propria of the tubules were thickened, and the tubules were smaller than normal. The section from the testis of the 14-year-old boy showed Sertoli cells only (fig. 1, *B*). In sections from the other 5 testes tubules with Sertoli cells only were present alongside tubules containing Sertoli cells and spermatogonia. In the section of the 13-year-old boy (fig. 2, *B*) an occasional prepuberal tubule persisted. In 2 other sections maturity in the tubules had progressed to primary spermatocytes. These sections were from the bilaterally retained testes of a man aged 25 who was the oldest in this series show-

TABLE 8. *Principal findings in microsections of 36 undescended testes of 34 patients*

Tissue	Age Obtained	No. Testes	Thick Basement Membrane	Seminiferous Tubules							Leydig Cells	Hyaline Degeneration
				Prepuberal	Spermatogonia		Primary spermatocytes	Spermatids	Spermatozoa	Sertoli cells only		
					Absent	Present						
Biopsy at orchiopexy	Puberal 13, 14, 17, 17	4	3	1	1	3	1, 17 yrs.	—	—	1, 14 yrs.	4	—
	Adult 25	2	2	—	—	2	2	—	—	—	2	—
Biopsy 4 to 10 years after orchiopexy	Puberal 17	1	1	1	—	1	1	1	1	—*	1	—
	Adult 18, 22, 23, 24	4	4	2	—	4	4	4	3	—*	4	—
Extirpated testes	Puberal 12, 15, 17	3	2	3	1	2	—	—	—	1, 17 yrs.	2	—
	Adult 18 to 27	11	11	4	11	—	—	—	—	11	11	—
	Adult 36 to 49	7	7	—	7	—	—	—	—	5	7	2
	Adult 54 to 73	4	4	1	4	—	—	—	—	1	2	3
Total		36	34	12	24	12	7	5	4	19	33	5

* Five-sixths of tubules showed Sertoli cells only.

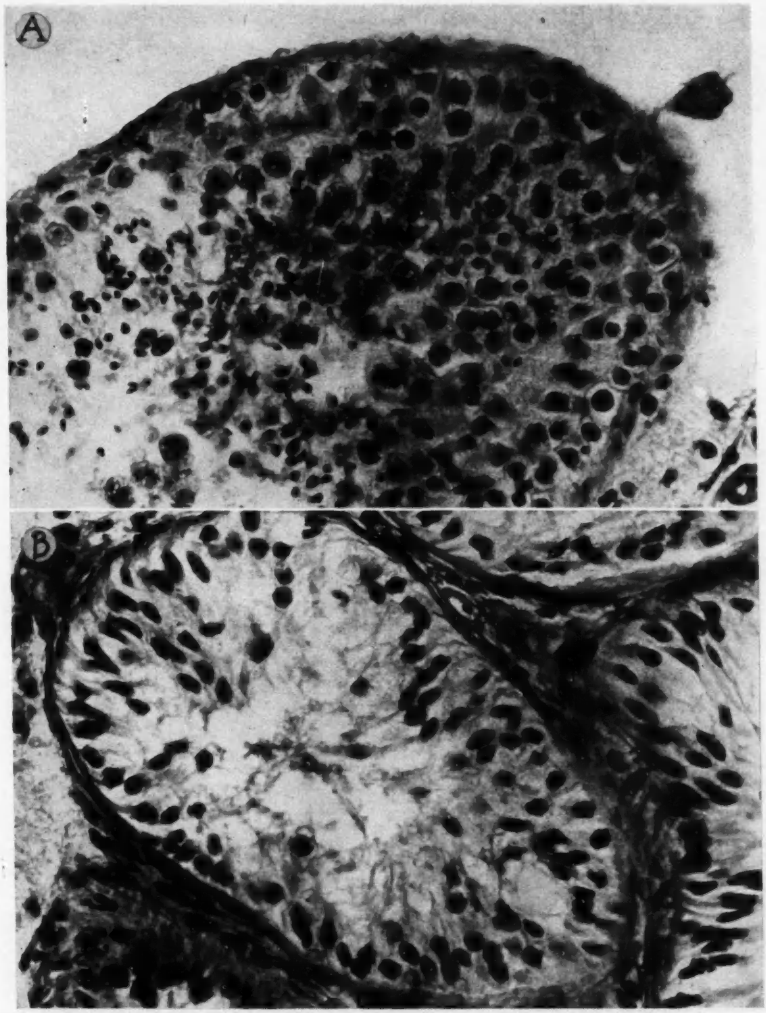

FIG. 1. *A*, normally descended testis showing spermatogenesis in a boy aged 14. *B*, mate brought down from external ring. Tubules contain Sertoli cells only.

ing some preservation of germinal elements (fig. 3). Leydig cells were preserved in all 6 sections.

2. *Biopsy after scrotal residence.* In this group there are sections of 5 testes placed by two-stage orchiopexies. Despite the scrotal residence of these testes there was evidence of degeneration along with normal tubules and preservation of Leydig cells. Though spermatogenesis was complete in 4 and arrested at the

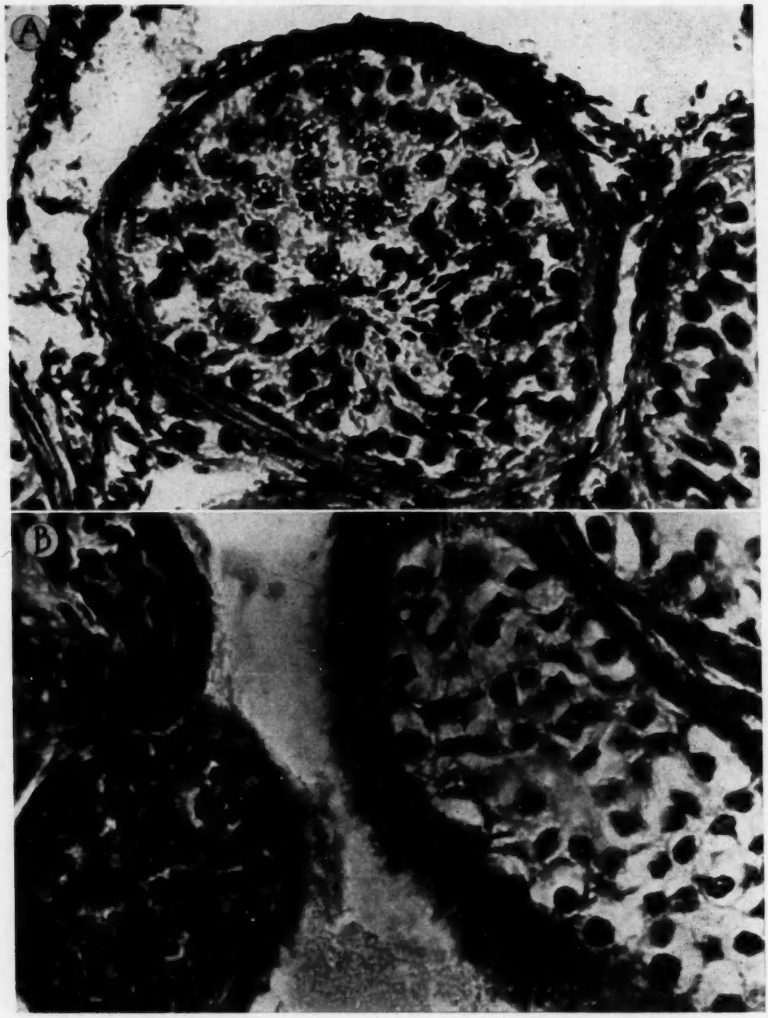

FIG. 2. *A*, normally descended testis, boy aged 13. Spermatogenesis together with prepuberal tubules and tubules with thick walls were seen. *B*, mate retained in pubopenile area showing prepuberal tubules and lagging maturation.

spermatid stage in 1, the spermatogenesis was focal, being present in only one-sixth of the tubules studied in each section (fig. 4).

Since the orchiopexies in this group were all two-stage procedures, it would seem that the degeneration resulted from injury to the blood supply during lengthening of the cord, or to narrowing, or, possibly, to spasm from the tension

incident to securing the testes to the thighs. However, for accurate assessment of the role orchiopexy plays in degeneration, it would be necessary to compare sections of the testes at the time of operation with those at followup. The value of biopsy studies is shown by the investigations of Charny, Hotchkiss, Nelson, Robinson and Engle, Rommer, among others.

3. *Tissue of testes removed.* Twenty-five testes are included here. Sections from

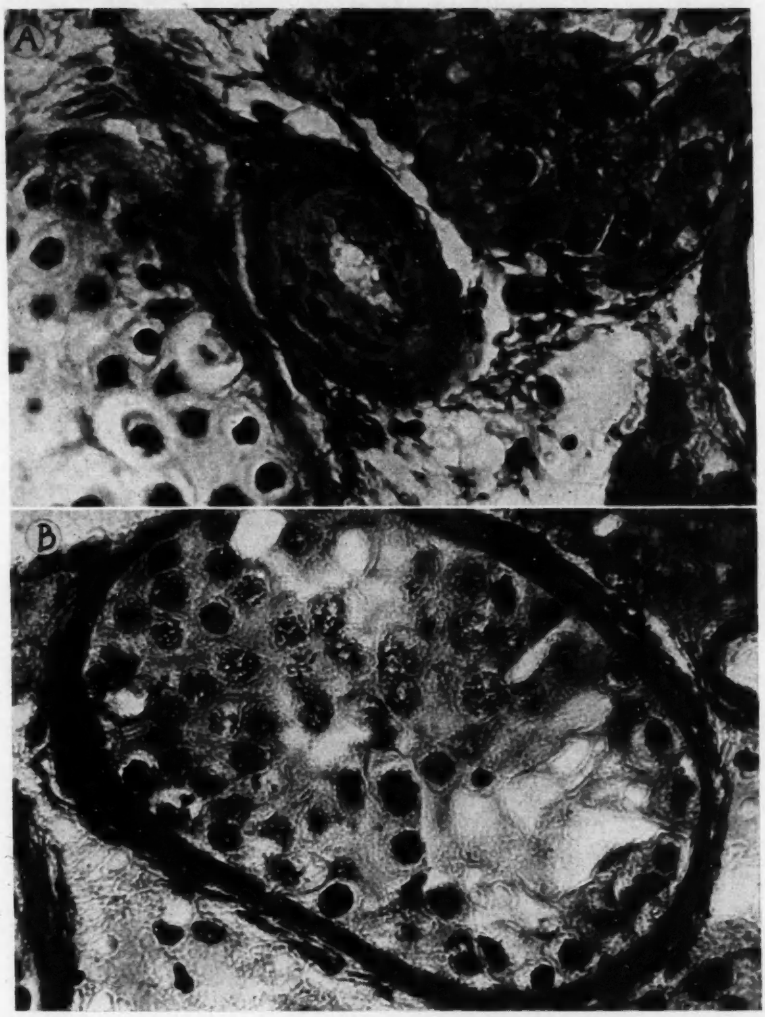

FIG. 3. *A*, testis retained in right canal in patient aged 25. Note preservation of spermatogonia and Leydig cell hyperplasia. *B*, mate retained in left superficial inguinal pouch. Germinal epithelium is preserved to primary spermatocyte stage.

FIG. 4. *A*, normally descended testis in patient aged 22. Spermatogenesis is present. *B*, mate brought down by Torek operation from canal at age 12. While this section, made at age 22, shows spermatogenesis, it was present in only one-sixth of tubules studied.

the testes of 3 puberal boys showed spermatogonia in 2, aged 12 and 15 (figs. 5 and 6, respectively). The section from the testis of the 17-year-old boy showed Sertoli cells only (fig. 6). Persistence of prepuberal tubules was evident in all 3 sections.

Sections of the testes of 22 adults, 18 to 73 years, all showed degeneration of germinal elements. In 5 the degeneration had progressed to destruction of the

Sertoli cells. Leydig cells were preserved in all but 2 sections. Prepuberal tubules persisted in 5 sections, indicating congenital defectiveness. The other instances of persistence of prepuberal tubules, shown in the table, could well be attributed to lagging maturity.

Of the 5 normally descended scrotal testes studied, sections of 4 showed no

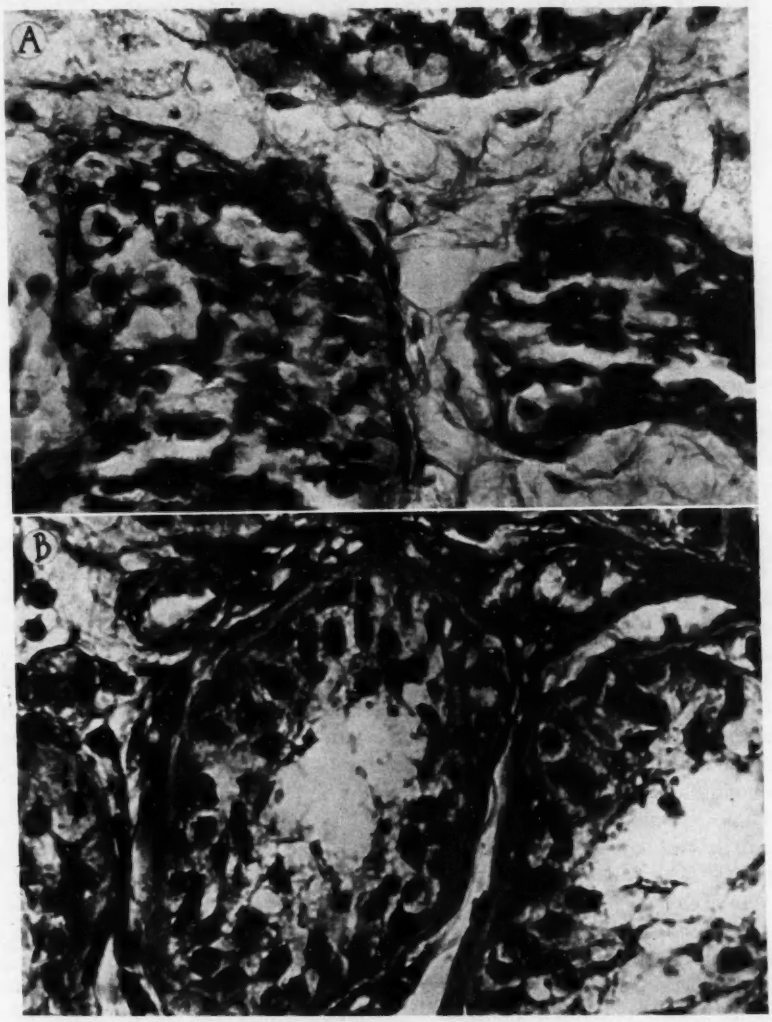

FIG. 5. *A*, testis removed from canal at age 12. Note prepuberal tubules indicating lagging maturation. *B*, mate removed from abdomen at age 15. Tubules are small. Spermatogonia are preserved.

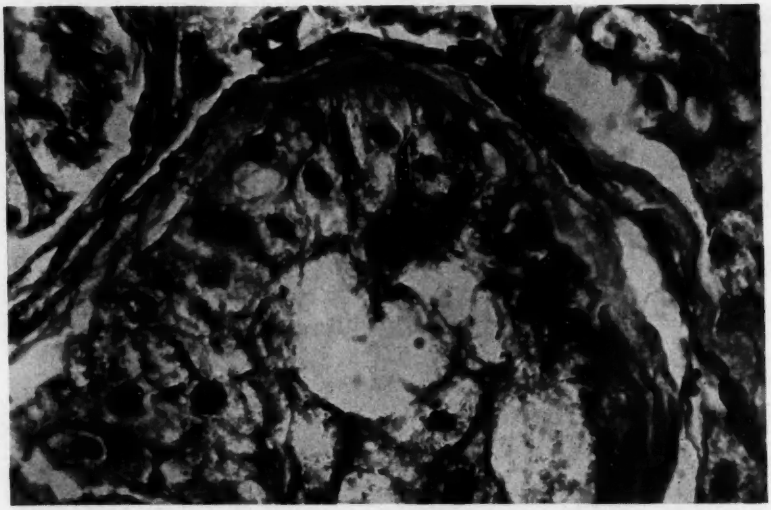

FIG. 6. Testis removed from canal at age 17 showing degeneration of the germinal epithelium.

abnormalities. The section of the fifth, that of a boy aged 13 (fig. 2), showed prepuberal tubules and thick tubular walls together with maturing tubules, as had been observed in his retained testis.

POSTOPERATIVE TREATMENT

Four patients are being maintained on testosterone by intramuscular and buccal absorption. The former is delatestryl (Squibb) in sesame oil. It is injected deep in the gluteal muscle every 6 weeks in doses of 1 cc or 200 mg. The latter is oreton-M (Schering's methyl testosterone), in 10 mg. tablets taken 1 to 4 times a day as necessary.

Of the 4 patients, 1 with unilateral retention had an orchiectomy at age 26. The testis, removed from the superficial inguinal pouch, contained a seminoma. This and his normally descended scrotal testis had atrophied after mumps in early childhood.

Three patients had bilateral retention clinically. On exploration 1 proved to have bilateral agenesis. The second, at age 39, had an orchiopexy on 1 side; the opposite testis was removed because of a seminoma. The third patient at age 22 had an orchiopexy; this testis, small at operation, was atrophied 11 years later. At this time, when he was 33 years old, the opposite side was explored and only a remnant of epididymis was found.

Chorionic gonadotrophin was used as an adjunct to orchiopexy in 1 patient who had poorly developed genitalia. After administration of the hormone there was improvement in genital development. The patient subsequently married and fathered 2 children.

FOLLOWUP

Of the 150 patients traced, 141 are alive; 9 are dead. Two, each 12 years old on admission, died at 22 and 23 years of age—1 was single, the other was married and had 1 child. The remaining 7, all adults on admission, died at ages ranging from 23 to 59. One was single, 6 were married and 5 of the 6 had fathered children. Of these 9 men, 2 had had bilateral retention which was treated; 7 had had unilateral retention which was treated in 2 instances and not treated as advised in 5.

Table 9 gives the length of the followup. This represents the interval from the time that one or both testes reached the scrotum or was removed, to the end of the followup on April 1, 1955 or death. The followup period for the adolescents still under observation and the adults who did not have treatment was computed from the time of admission.

Of the 141 living patients, 75 responded to a questionnaire, 66 came in for re-examination. The 4 patients who had seminomas have now been alive 5, 6, 6½ and 15 years respectively.

Clinical findings. Evaluation of the size, position and consistency of the testes that had descended spontaneously or were brought down by orchiopexy is shown in table 10. Whereas the position was better after the two-stage orchiopexy, the size and consistency were better after the one-stage procedure. The testes that had descended spontaneously showed the greatest number of good results in all

TABLE 9. *Length of followup*

Followup Period	Total Pts.	Side Involved	
		Bil.	Unil.
6 to 11 months	19	4	15
1 to 9 years	54	13	41
10 to 19 years	45	16	29
20 to 29 years	28	13	15
30 to 33 years	4	3	1
Total	150	49	101

TABLE 10. *Clinical findings on followup examination*

Status of Testes	Spontaneous Descent			Orchiopexy					
	44 Testes			1 Stage 59 Testes			2 Stage 27 Testes		
	Normal	%	Abn.	Normal	%	Abn.	Normal	%	Abn.
Position	42	95.35	2	42	71.19	14	25	92.59	—
Size	40	90.7	4	30	50.85	26	11	40.74	14
Consistency	42	95.35	2	38	64.41	18	14	51.85	11
Not palpable because of atrophy or subsequent orchiectomy	—	—	—	—	—	3	—	—	2

TABLE 11. *Status of testes before reaching scrotum and on recent followup after residence in scrotum*

Status on Admission		Age when Testes Reached Scrotum		Size after Reaching Scrotum			
				23 by Spontaneous Descent		51 by Orchiopexy	
Size	No. testes	No.	Age group	No. normal	No. small	No. normal	No. small
Small	60	9	Prepuberal	1	—	7	1
		42	Puberal	14	3	11	14
		9	Adult	—	—	—	9
Normal	14	5	Prepuberal	4	—	1	—
		6	Puberal	—	—	3	3
		3	Adult	—	1	2	—
Total	74	14	Prepuberal	5	—	8	1
		48	Puberal	14	3	14	17
		12	Adult	—	1	2	9

three respects. Of the 4 testes that were small after spontaneous descent, 3 had come down at puberty; the fourth came down at age 21 and was atrophied. According to Zide, the adult human testis does not undergo any appreciable compensatory hypertrophy after atrophy or removal of its mate.

Six testes retracted after one-stage orchiopexies and herniorrhaphies (5 elsewhere) on patients aged 2, 5, 5, 6, 11 and 49 at the time of operation. Two other testes, 1 attached in the scrotum and 1 left attached to the thigh, had atrophied and were impalpable.

An attempt was made to compare the size of the testes before and after they reached the scrotum. Records of the size on admission were available for 103 testes, 29 of which were either removed, not yet in place, or in patients not traced. The 74 left for comparison are shown in table 11. On the whole, the size was better after spontaneous descent. But the younger patients exhibited better development after both spontaneous descent and orchiopexy than the adults.

The cremaster reflex, which one would expect to approach normal after spontaneous descent, has been absent or weakly positive in patients examined thus far. Absence of the cremaster reflex is expected after orchiopexy because the cremaster muscle is removed during the operation.

Fertility in married patients with bilateral retention. Of the 49 patients with bilateral retention who were traced, 24 or 48.98 per cent were married; 14 or 28.57 per cent were single adults; and 11 or 22.45 per cent were adolescents (table 12).

Fifteen of the married men had children. The fate of the testes of these men is shown in table 13. In all but 1 man, 1 or both testes were in the scrotum by puberty.

The highest incidence of fertility was among the 13 men whose testes had both descended spontaneously before or during puberty. Six were married, and all were fertile, having fathered from 1 to 4 children.

Nine men had spontaneous descent of 1 testis. Of these 6 are married and 4 have had children. Of the 4 fertile men:

In 1, spontaneous descent occurred at the age of 8 and shortly thereafter the opposite testis was brought down by a one-stage orchiopexy. He is now 29 years old and has 1 child. Both testes probably contributed to his fertility.

In the second patient the testes descended at the age of 11; the mate was removed from the abdomen at age 23. Now 34 years old he has 3 children. In the third man the testis descended at age 14. Exploration of the opposite testis at the same age disclosed agenesis. Now 46 years old, he has 8 children. In both these men spontaneous descent was responsible for the fertility.

In the fourth man descent did not occur until he was 21 years old, at which time the testis, arrested at the external ring, was atrophied, as already pointed out. His opposite testis had been brought down from the external ring by a one-stage orchiopexy when he was 8 years old. Now 36 years of age, he has 4 children. In view of the descent of 1 testis after puberty and early placement of the opposite testis by a one-stage orchiopexy, his fertility can be ascribed to the operation.

TABLE 12. *Summary of marital status on followup of patients traced*

Status of Patients	51 Patients with Bilateral Retention		102 Patients with Unilateral Retention	
	No. pts.	%	No. pts.	%
Traced	49		101	
Married	24	48.98	61	60.39
with children	15	62.5	47	77.05
without children	9	37.5	14	24.19
Single adults	14	28.57	18	17.82
Adolescents	11	22.45	22	21.78

TABLE 13. *Evaluation of fertility of 15 married men with bilateral undescended testes*

Fate of Testis	Total Pts.	No. Married	No. with Child.	%	Age of Fertile Men at Operation or Descent of Testes		
					Prepub.	Puberal	Adult
Bil. spontaneous descent	13	6	6	100.00	2	4	—
Bil. orchiopexy	18	9	4	44.44	—	4	—
1 side spont. descent, 1 side orchiopexy	6	4	2*	50.00	2	—	—
1 side spont. descent, 1 side orchiectomy	2	1	1	100.00	—	1	—
1 side spont. descent, 1 side agenesis	1	1	1	100.00	—	1	—
1 side orchiopexy, 1 side orchiectomy	4	2	1†	50.00	—	—	1
Both put in abdomen, rings closed	1	1	—	—			
Total	45	24	15	62.50	4	10	1

* Patient had orchiopexy at 8 and descent at 21. Orchiopexy likely contributed to fertility.

† Both operations done at age 53. Son born when patient 41. Orchiopexy cannot be credited with producing fertile testis.

Of the men who had bilateral orchiopexies, 9 are married. Four have had children—1, 2, 2 and 3, respectively. Each of the 4 men was operated on during puberty. Each had a one-stage orchiopexy. Adding to these the man who had had a one-stage orchiopexy on 1 side at age 8 and spontaneous descent on the opposite side at age 21, fertility can be credited to one-stage orchiopexy in 5 men.

In another man who was operated on after puberty orchiopexy cannot be credited with contributing to his fertility. He had had a son when he was 41, at which time 1 testis was in the canal and the mate in the abdomen, as operation at age 53 proved.

In MacCollum's series of 11 patients having bilateral orchiopexies 6 had children. Coley reported paternity in a man who had had orchiopexy on 1 side at age 30 and orchiopexy on the opposite side at age 45. Bishop reported paternity in 1 patient after spontaneous descent of the right testis at age 16 and removal of the left testis at age 20.

Infertility in married patients with bilateral retention. In table 14 an attempt has been made to explain the possible reasons for the infertility of 9 married men with bilateral undescended testes.

Cases 1, 5 and 9: Clinically all 3 patients showed failure of germinal and Leydig cells. One patient (case 1) was first seen here at age 18, 10 years after both testes had been put in the abdomen and the rings closed. Presumably shortness of the cords had dictated this management. Two patients (cases 5 and 9) were operated on after puberty.

Cases 2 and 3: Despite the spontaneous descent of 1 testis by age 12 in each man, ejaculate counts showed diminished spermatozoa counts. Neither man consented to biopsy.

Case 4: Bilateral one-stage orchiopexies done at a suitable age did not preserve the testes. The testicular failure, indicated by high gonadotrophin surveys, may be due either to intrinsically defective testes or to embarrassment of the blood supply at operation.

Cases 6, 7 and 8: In these, bilateral orchiopexies were done after puberty when, it is presumed, the germinal epithelium has begun to deteriorate. In 1 patient (case 7) biopsy at age 24 showed focal spermatogenesis, but the ejaculate showed aspermia which would indicate a blocked tubular system. In another patient (case 6) biopsy and orchiopexy at age 25 disclosed maturation to primary spermatocytes. The ejaculate on one occasion after operation showed a few nonmotile spermatozoa. Still another patient (case 8) had small testes and the ejaculate showed aspermia.

Probability of fertility in single adults with bilateral retention. Of the 14 single adults, 7 must be eliminated from the evaluation of potential fertility because of: gonadal anomalies which were bilateral in 2 patients and in 1 patient associated with an atrophied testis on the opposite side; confinement in a mental institution, 1; being a priest, 1; death, 2.

Another patient, now 29 years old, has grand mal epilepsy and is mentally retarded. He will probably not marry. In still another patient prognosis must be guarded. Both testes were brought down from the external rings by two-stage

TABLE 14. *Evaluation of infertility in 9 married men with bilateral undescended testes*

Case	Fate of Testes	Age at Operation or Descent of Testes			Follow-up	
		Prepub.	Puberal	Adult	Present age	Comment
1	Both put in abdomen, rings closed	8 & 8	—	—	49	Eunichoid appearance
2	1 side spontaneous descent, 1 side orchiopexy 1 stage	—	12 & 13	—	33	Few spermatozoa in ejaculate; no scrotal development; obesity
3	1 side spontaneous descent, 1 side orchiopexy 1 stage	—	12 & 25	—	33	Nonmotile spermatozoa in ejaculate
4	Bilateral orchiopexy 1 stage	—	11 & 11	—	27	Gonadotrophic surveys high, indicating testicular failure
5	Bilateral orchiopexy 1 stage	—	—	21 & 21	33	Hypogonadotrophic hypogonadism
6	Bilateral orchiopexy 1 stage	—	—	25 & 25	25	Biopsy—primary spermatocytes. Few nonmotile spermatocytes in subsequent ejaculate
7	2 stage	—	—	18 & 18	24	Biopsy—focal spermatogenesis. Aspermia, indicating blocked tubular system
8	2 stage	—	—	25 & 25	29	Aspermia
9	1 side orchiopexy 2 stage, 1 side orchiectomy	—	—	39 & 39	45	Seminoma; hypogonadism, hypothyroidism; maintained on testosterone

orchiopexies when he was 15 years old. Recent recheck, at age 23, showed both testes to be soft. Biopsy at this time disclosed not only areas of focal spermatogenesis but also areas of degeneration as well as late prepuberal tubules which indicate immaturity.

Thus, of the 14 single adults, fertility is probable in only 5. Of these, 4 men, now 18, 19, 29 and 34 years old, had bilateral spontaneous descent, all of the testes reaching the scrotum by age 12. The fifth patient, now 21, had spontaneous descent on 1 side at age 9 and a two-stage orchiopexy on the opposite side at age 13. Recent followup disclosed that the testes of all 5 patients were of normal size and consistency and at the bottom of the scrotum.

Probability of fertility in adolescents with bilateral retention. Of the 11 adolescent patients, 2 are now being treated for perineal hypospadias, at the ages of 10 and 11.

Fertility is probable in the remaining 9 patients. In 3 both testes descended spontaneously, reaching the scrotum at the ages of 9 or 12. One had spontaneous descent on 1 side at the age of 9 and a two-stage orchiopexy shortly thereafter. Four patients had bilateral orchiopexies—one-stage procedures in 2 patients and two-stage procedures in the other 2 patients. In 3 patients the testes were brought down at age 2, 8, and 9, respectively. In the fourth patient 1 testis was brought down at age 13, the mate at age 17. Biopsy at age 17 showed maturation to spermatids in the testis brought down at 13 and to the stage of primary spermatocytes in the testis brought down at 17.

Recapitulation of fertility and infertility in patients with bilateral retention. From the foregoing it can be stated that of 49 patients with bilateral undescended testes who have been traced:

Fertility was established by paternity in 15 patients—in 6 after bilateral spontaneous descent, in 4 after one-stage orchiopexies, and in 5 as explained previously.

Fertility is possible in 16 patients—1 married man, because tissue studies showed primary spermatocytes and his ejaculate after bilateral one-stage orchiopexies showed nonmotile spermatozoa; his testes may show further improvement after scrotal residence; 6 single adults and 9 adolescents in whom spontaneous descent had occurred or orchiopexy had been done at a favorable age which brought one or both testes to the scrotum not later than puberty.

Fertility is unlikely in 18 patients—8 married, 8 single adults, and 2 adolescents—for reasons already stated.

Fertility in married patients with unilateral retention. Of the 101 patients with unilateral undescended testes who were traced, 61 or 60.39 per cent are married; 18 or 17.82 per cent are single adults; and 22 or 21.78 per cent are adolescents (table 12).

Of the 61 married men, 47 or 77.05 per cent have had children. Table 15 shows the incidence of fertility according to the fate of the undescended testis. In 11 men paternity occurred after the testis reached the scrotum—in 2 by spontaneous descent at puberty; in 9 by orchiopexy done before puberty in 2, during puberty in 6 and after puberty in 1. The subsequent development of these testes in the scrotum may have contributed to the fertility. Three other men, first seen at puberty, had orchiectomy, removal of epididymal remnants, no treatment, respectively. The 3 testes of these men did not contribute to fertility. The remaining 23 patients all had had children prior to admission so their retained testes presumably did not contribute to fertility.

As table 15 shows, further, only 8 of the 47 fertile men had come for treatment of their retention, and all 8 were seen before or during puberty. The others had come in because of hernia, pain, a mass, or complaints unrelated to the genitalia.

Hansen found that men with 2 testes produce on an average twice as many spermatozoa as men with only 1 testis; that operation usually does not make the operated testis produce a significant number of spermatozoa; that in unilateral retention "the normally descended testis must be considered as capable of function as either of the 2 testes in normal men."

TABLE 15. *Evaluation of fertility of 47 married patients with unilateral undescended testes*

Fate of Testes	Total Pts.	No. Married	No. with Child.	%	Age at Operation, Descent or Admission			Chief Complaints			
					Prepub.	Puberal	Adult	Retention	Hernia	Pain, orchitis tumor	Other conditions
Delayed descent	8	3	2	66.67	—	2	—	2	—	—	—
Orchiopexy	35	12	11	91.67	2	6	3*	4	7	—	—
Secondary orchiectomy	3	3	2	66.67	1†	—	1†	—	2	—	—
Primary orchiectomy	30	23	16	69.56	—	1	15	—	11	2	3
Exploration or removal, epididymal remnants	7	5	4	80.00	—	1	3	1	—	1	2
No treatment	15	15	12	80.00	—	1	11	1	4	—	7
Total	98	61	47	77.05	3	11	33	8	24	3	12

* Patients had had children prior to admission.

† Age at primary orchiopexy.

Infertility of married patients with unilateral retention. Despite having 1 scrotal testis, 14 of the married men have not had children (table 16). Two had small scrotal testes on palpation. Biopsy of 1 of the 2 testes, in a patient aged 32, showed focal spermatogenesis. Studies of his ejaculate showed no spermatozoa, which indicates a blocked tubular system.

The remaining 12 patients had apparently normal scrotal testes on palpation, and should be fertile from that standpoint. Of these, 2 had retained testes that reached the scrotum at an age favorable for complete development. The retained testes of 6 patients were removed, 1 testis was not found on exploration, and 3 were not treated. Possibly contributing to the infertility of 4 patients were congenital defects in retained testes of 3 and a defect in the scrotal testis of 1. Three patients have uncorrected retention. Additional defects may be present in their testes.

Probability of fertility in single adults with unilateral retention. Of the 18 single adults with unilateral retention, 3 are priests. Among the other 15 patients, 7 had unilateral orchiopexies at a favorable age, and scrotal residence of these testes may contribute to fertility. Fertility of the remaining 8 patients will have to depend on the scrotal testis alone since in 1 patient the retained testis was brought down at age 25 and the testes of the other 7 patients were removed. In this group there is 1 congenital anomaly in a retained testis.

Probability of fertility in adolescents with unilateral retention. Of the 22 adolescents with unilateral retention, 1 had agenesis and 1 is still under treatment. The testes of 20 patients reached the scrotum by the age of 12 (16 by orchiopexy, 4 by spontaneous descent). These testes should contribute to the fertility of the patients.

TABLE 16. *Evaluation of probable infertility in 14 married men with unilateral undescended testes*

Fate of Testes	Age Operation or Admission			Followup	
	Prepub.	Puberal	Adult	Present age	Status of testes
Spontaneous descent	10	—	—	22	Position, size, consistency normal
Orchiopexy, 2 stage	—	15	—	23	Position, size, consistency normal
Primary orchiectomy	—	—	18	24	No spermatogonia
	—	—	21	32	Retained testis—no spermatogonia; biopsy scrotal testis showed focal spermatogenesis. No spermatozoa in ejaculate, indicating blocked tubular system
	—	—	42	46	No spermatogonia
	—	—	23	46	Section not available
	—	—	26	49	No spermatogonia
	—	—	37	46	No spermatogonia
	—	—	65	71	Congenital defect
Secondary orchiectomy	—	—	37	53	Attached to thigh 16 years. Atrophied. No spermatogonia.
Epididymal remnants removed	—	—	18	28	Agenesis
No treatment	—	—	18	40	Testis still retained
	—	—	53	59	Testis still retained at death
	—	—	59	64	Testis still retained

Recapitulation of fertility and infertility in patients with unilateral retention. In a total of 101 patients with unilateral undescended testes, the retained testis:

Presumably contributed to the fertility of 47 men who fathered children.

May contribute to fertility in 29 men.

Will not contribute to fertility in 25 because of congenital defects and prolonged retention.

DISCUSSION

Factors in development. The process of development and descent of the testis is, briefly, as follows (Grant; Hamilton, Boyd and Mossman; Wells (1943, 1944)):

The structures composing the body of the testis originate in the mesothelium, or peritoneum, covering the medial aspect of the urogenital fold (Arey; Kollmann). Migrating into the developing tubules are primitive germ cells (spermatogonia) which come from the yolk sac by way of the mesentery (Witschi). The excretory apparatus originates in the lateral aspect of the urogenital fold (Arey; Kollmann). Uniting the testicular structures and the excretory apparatus is the rete testis which is a gonadal anlage (Young). Faulty integration of any one of these phases in development causes defective testes.

Developing simultaneously with the testis, the mesothelium forms two folds. The upper, containing the spermatic vessels, unites the superior border of the testis to the diaphragm. The lower, commonly called the gubernaculum, unites

the epididymis and, indirectly, the inferior border of the testis to the abdominal wall at the site of the developing inguinal canal. By the seventh month the testis lies at or near the inguinal ring.

The scrotum is evident in the twelfth week as bilateral swellings. These coalesce to form the single structure.

In preparation for the descent of the testis to the scrotum, the abdominal wall evaginates (in the fourth month, according to Wells) to form an inguinal bursa. Corresponding to the layers of the abdominal wall, the bursa is composed of "the external spermatic fascia (intercolumnar fascia), the middle spermatic fascia (cremasteric muscle and fascia), the internal spermatic fascia (infundibuliform fascia or tunica vaginalis communis)"—or transversalis fascia—"and the peritoneum (tunica vaginalis proprius)."

The processus vaginalis, communicating with the abdominal cavity, invests all but the posterior surface of the testis and cord. This, together with the other three layers of the bursa, precedes the testis into the scrotum—all these structures normally acting as a single unit.

Frequency of retention. In February, March and April of 1955 I checked the infants born at St. Vincent's hospital and under my supervision those born at Wilcox Memorial hospital were also checked. During this period 656 full term and 33 premature infants were delivered in the two hospitals. Of the 33 premature infants, 5 had incompletely descended testes, or 15.15 per cent. Of the 656 full term infants, 14 or 2.1 per cent, had undescended testes, being bilateral in 5 and unilateral in 9. This is lower than the 10 per cent in 450 full term infants given by Hofstätter. In 2 premature and in 1 mature infant both testes descended by the time they were taken home. During the same period there were 14 stillbirths.

Of 3,197 boys from 5 to 18 years of age, in the series reported by McCutcheon, undescended testes were present in 204 or 6.08 per cent. Among 1,301 boys between the ages of 11 and 18, Chastain and Newlin noted undescended testes in 27 or 2.08 per cent. In Johnson's series of 31,609 boys aged 7 to 17 years, 544 had undescended testes, approximately 17 per 1,000 or 1.72 per cent. And among registrants examined for military service during World War II, the prevalence rate of undescended testes was 4.83 per 1,000 or 0.4 per cent*

None of the boys in the series of McCutcheon had had treatment. The boys in the series of Chastain and Newlin had had chorionic gonadotrophin. In Johnson's series 5 boys had hormone therapy and 14 had orchiopexies; boys between 11 and 13 years had no treatment. Data are not available on the number of registrants for military service who might have had either chorionic gonadotrophin or orchiopexy.

Factors in delayed descent. The decreasing prevalence of clinically undescended testes with progressive age is evidence in support of delayed spontaneous descent. McCutcheon, Johnson, Chastain and Newlin, Mimpriss, Thompson et al. among others report instances of delayed descent with and without hormone therapy.

Studies are lacking relative to the gross and microscopic appearance of testes

* Division of Statistics, Department of The Army Office of Surgeon General: Personal communication from E. L. Hamilton.

that descend spontaneously. The assumption is that they approximate the normal when they reach the bottom of the scrotum before or at puberty. These testes, failing to respond to the surge of gonadotrophins at birth, come down at puberty when the pituitary gland releases gonadotrophins and, in some instances, respond to administration of chorionic gonadotrophin before puberty, as demonstrated here and elsewhere.

In each of the testes descending late, as in the normal, the external spermatic fascia and the bursa which it covers have prepared a pathway for descent. At least, the pathway extends to the lowest level to which the testis descends temporarily or can be manipulated. But in the testis that must be brought down surgically the spermatic fascia may have become a barrier instead of a pathway, possibly because it becomes detached from its scrotal attachment or because it has had an aberrant attachment elsewhere than in the scrotum to begin with.

Factors in retention. Failure of the testes to descend may be due to imperfections at any stage of development. These may be manifested by defectiveness in the gubernaculum, adhesions of the bursa, short blood vessels, disproportionate size of the testis and the canal, and deficiency in the testis itself, as observed by Hunter, in 1786, and other investigators since his time (Bland-Sutton; Nelson; Sohval).

In the retained testes, Scarpa's fascia, or the deep membranous layer of the superficial fascia, and its perineal portion, Colles' fascia, become of particular importance because they are incorporated in the formation of pouches in which the testes may be trapped in their descent to the scrotum. A superficial inguinal pouch was described by McGregor and later by Browne.

The pouch defined by Browne, lying between Scarpa's fascia and the external oblique, includes all the space superior and lateral to the external ring and in general corresponds to the space into which the testis goes when it is manipulated out of the scrotum onto the abdomen. The pouch described by McGregor is smaller and limited to the area behind the reflected portion of Scarpa's fascia, or Scarpa's ligament as he calls it. Two other pouches pointed out by McGregor are the "crural" and the "superficial perineal" pouches. In addition, he described a "third inguinal ring" formed posteriorly by Scarpa's ligament and anteriorly by the fusion of Scarpa's and Colles' fascias.

Opinions vary as to the role the gubernaculum plays in descent. John Hunter, who is credited with discovering this controversial structure, described it in 1786 as "the ligament, or gubernaculum testis, because it connects the testis with the scrotum, and directs its course in its descent." Lockwood, in 1887 and 1888, expressed the belief that it fanned out to produce five strands of attachment and that it was capable of traction. Richard Hunter, in 1926, stated that in the newborn the gubernaculum is "not attached to the skin of the scrotum and the testis cannot be drawn from the abdominal cavity to the scrotum by its contractions." Pearson and Boots, in 1954, demonstrated that the "gubernaculum" extends through the subcutaneous inguinal ring where it fuses or is continuous with a fascia-like layer resembling in position the deep layer of the superficial fascia. Wells and State studied 4 patients subjected to orchiopexy and concluded

that what surgeons regard as the gubernaculum is actually "a ligament of connective tissue" blending with the external spermatic fascia. A transverse section through this structure in one of my patients showed both smooth and striated muscle fibers as well as connective tissue (fig. 7).

From my observations at orchiopexy, I am inclined to believe that this process, which covers the bursa and continues beyond it, is an extension of the external

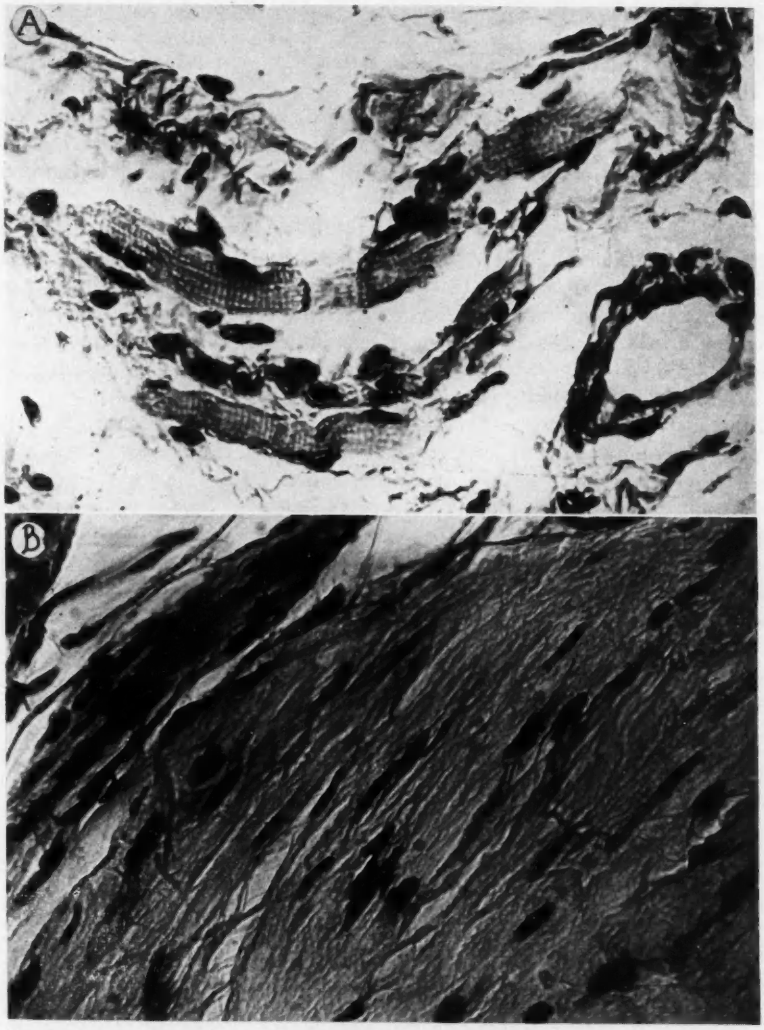

FIG. 7. Spermatic fascia projecting beyond bursa sectioned at point of its attachment in the perineal pouch. Both striated muscle (*A*) and smooth muscle (*B*) were present.

spermatic fascia. I have seen it in an adult of 73 years as a single tubelike structure extending from the caudal end of the bursa to the bottom of the scrotum where it was fixed, and traction on it evaginated the scrotum. The presence of the outer testicular investment in the scrotum and the simultaneous arrest of the processus vaginalis and testis at a higher level would suggest that successful descent of the testis is dependent on more than a guiding structure (fig. 7). This is the only patient with retention in whom I have observed a patent "third inguinal ring."

As a single structure I have seen it fixed to the lateral border of Scarpa's fascia at the third inguinal ring and to Scarpa's fascia at the level of the fossa ovalis (fig. 8). I have also seen it, again as a single structure, directed laterally into the depths of what McGregor designated as the superficial inguinal pouch. And, yet again as a single structure, I have seen it directed over the pubis and fixed in the perineal pouch.

I have seen it split into bands directed most often laterally and fixed to Scarpa's fascia at the level of the fossa ovalis. And I have seen it directed medially toward the spine of the pubis (fig. 9). In a patient of 26 years the testis clinically was freely movable in the superficial inguinal pouch, described by Browne, and at operation the bursa with its covering of spermatic fascia was not attached anywhere within the pouch but was lying free underneath Scarpa's fascia (fig. 10). It is these deviations that give rise to retention in various positions.

In addition to the aforementioned, imperfections of other types are discernible at practically all operations for correction of retention. I have seen them at every level of arrest. For instance, at the abdominal level in 1 patient a testis had peritoneal attachments but no demonstrable processus vaginalis. In other patients, a long mesorchium had allowed the testis to migrate to and from the canal. In the canal, I have seen a testis which had turned back over the internal oblique (fig. 11). Lower in the canal I have encountered changes ranging from an absence of the external ring to a partial opening through bands of the external

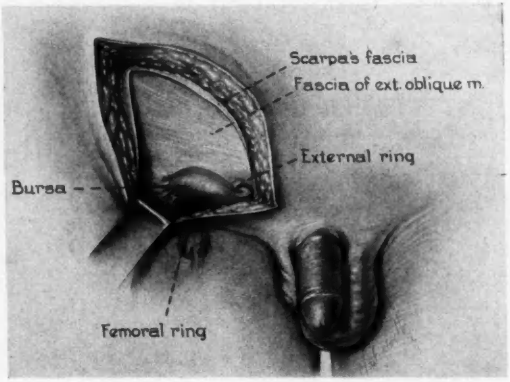

FIG. 8. Boy 6 years old. External spermatic fascia attaching bursa to Scarpa's fascia above external ring. Note undeveloped scrotum on involved side.

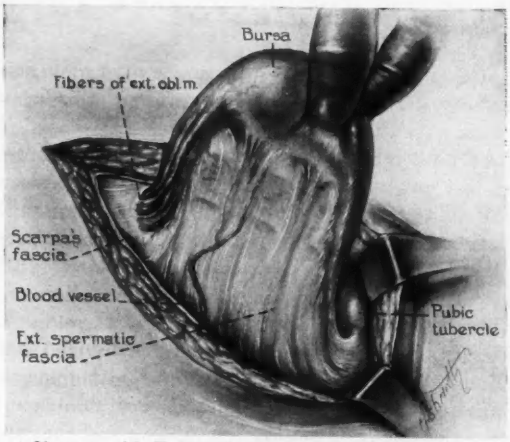

FIG. 9. Patient 29 years old. External spermatic fascia attached to pubic tubercle

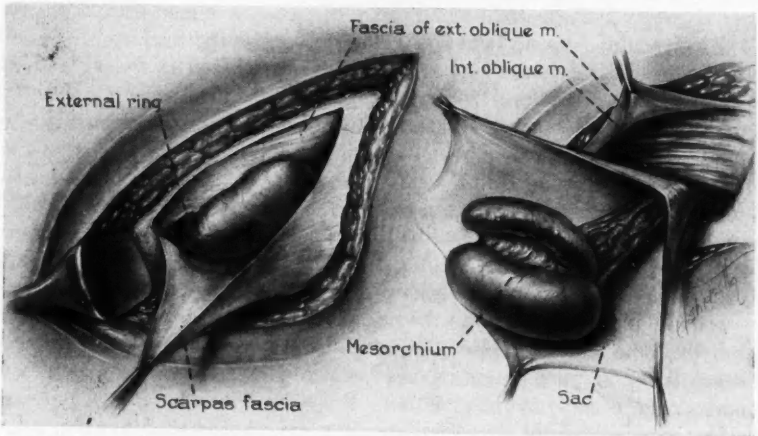

FIG. 10. Left testis in superficial inguinal pouch between Scarpa's fascia and external oblique

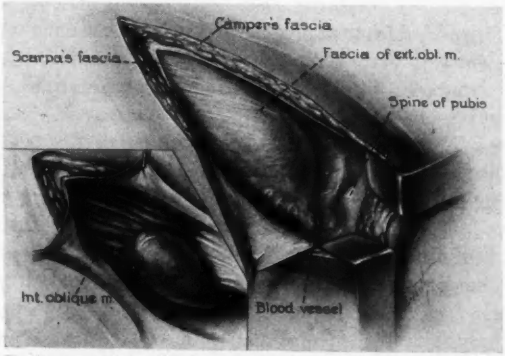

FIG. 11. Patient aged 25. Right canalicular testis. External ring is absent

spermatic fascia. Below the level of the external ring I have observed that the external spermatic fascia had become a barrier. It is in this location that testes frequently turn back over the external oblique fascia.

An observation I have made in removing normally descended scrotal testes for carcinoma of the prostate is of interest in this connection. The external spermatic fascia covering the testis and cord is closely adherent to the dartos of the scrotum at a point corresponding to the juncture of the lower pole of the epididymis and the beginning of the vas. The testis cannot be lifted out of the scrotum until the adherent spermatic fascia is separated from the dartos. This is contrary to the observations of Richard Hunter in the newborn.

Factors in the damaging effects of retention. It has been shown that the temperature in the peritoneal cavity is higher than in the scrotal cavity (Benedict and Slack; Hunter; Moore; Moore and Quick), and that the cooler scrotum is a thermoregulator for the testis (Crew; Moore; Moore and Quick). The vascular pattern of the testis itself also acts as a thermoregulator because the heat of the spermatic artery is dissipated as it passes between the cooler veins of the pampiniform plexus and as its tributaries course over the free surface of the testis before giving off deep branches to supply the parenchyma (Harrison and Barclay; Harrison and Weiner [1948, 1949]). The dartos also plays a role in the thermoregulating mechanism of the scrotum by relaxing in response to heat and contracting in response to cold.

Moore, and Moore and Quick demonstrated the damaging effect of heat on the testis. Working with guinea pigs they showed that degeneration of the germinal epithelium occurs when the adult testis is placed in the peritoneal cavity and that if spermatogonia are still present regeneration occurs after replacement in the scrotum. Wangensteen, using dogs, made the same observations when he placed the testis in the peritoneal cavity or the inguinal area. He also noted similar, though limited, changes when the testis was simply lifted out of the scrotum and immediately replaced, which demonstrates the sensitivity of the maturation process to manipulation. When he transplanted the immature testis degeneration did not occur. Badenoch expressed the belief that the descent of the testis from the abdominal cavity represented its need for the lower temperature of the scrotum.

Histologic studies added further proof of the deleterious effect of the abnormal position. Cooper showed that after the third year the retained testis exhibits increase in the intertubular fibrous tissue which may go on to fibrosis as puberty approaches as well as to decrease in size and " 'apparent' " decrease in the number of tubules. These observations have been substantiated by the studies of Nelson. Robinson and Engle noticed that scrotal and undescended testes are similar until the age of 5. Thereafter growth of the retained testis is retarded.

Cooper also made the significant observation that "at whatever position the testis is arrested, and at whatever pre-adolescent age it is examined, the essential elements of the gland, i.e., spermatogonia and undifferentiated cells, are, if not throughout the gland, certainly in many parts, identical in position, structure and relationship with the scrotal testes of the same age." That is to say, that to-

gether with degenerative changes "healthy spermatogonia, undifferentiated cells and cells of Sertoli may be present." This observation was evident in the present study.

The more recent extension of interest in the histologic structure of the testis—seeking to evaluate the normal at different ages from the fetus to the adult (Albert, Underdahl, Greene and Lorenz; Charny) as well as the retained (Nelson; Sniffen; Sohval)—will doubtless lead to a better answer of what can be expected from placement.

Factors in corrective measures. The first orchiopexy is attributed to Koch who, according to Rosenmerkel, in 1820, unsuccessfully used a suture to fix the testis to the fundus of the scrotum. Schüller, in 1881, recognized the need of lengthening the cord before placing the testis in the scrotum, using a stitch to secure the testis. Bevan, in 1903 and 1929, carried the principle of achieving more length further by removing the vaginal process from the cord and used a purse-string suture at the top of the scrotum to keep the testis in its new position. Ombredanne, in 1927, devised a trans-scrotal fixation operation. Browne, in 1949, brought the testis through a fascia overlying the pectineus muscle and left it free in the scrotum. All these were one-stage procedures.

Recognizing the principle of fixation, Keetley, in 1905, and Torek, in 1909, independently introduced a two-stage procedure. These differed in that Keetley sutured the "gubernaculum" to the fascia of the thigh whereas Torek sutured the tunica of the testis to the thigh.

The many operations developed subsequently have been modifications chiefly with regard to refinements in the technique of lengthening the cord; the manner of fixation; and devices for traction (Abrahamson; Cabot and Nesbit; Caucci; McKenna and Ewert; Ormond, Cothran and Singiser; Wangensteen; Wolfson and Turkeltaub).

Orchiopexy dominated the field of treatment until 1930 when Shapiro reported descent of the testes in adolescent boys after the use of "präharmon," the proprietary name for chorionic gonadotrophin. Subsequent clinical and experimental data support the view that chorionic gonadotrophin causes or accelerates descent of the testis, that it increases not only the size of the testis and all cord structures but widens the canal and stimulates scrotal growth.

In this study it was noted that in some patients, testes failing to respond to hormone stimulation prior to puberty responded to the surge of hormones at puberty. Such testes raise 2 questions: 1) Was the dose of hormone given adequate? 2) Will the doses suggested now insure descent?

Engberg observed no untoward reaction in giving the hormone to newborn babies in amounts of 1,000 international units per injection. Robinson and Engle suggested administration of the hormone between the ages of 2 and 5 in doses of 4,000 to 5,000 units daily for 3 days and advised that if descent did not occur within a week operation should be done. Smith favored doses of 500 to 1,000 units 3 times a week for 6 to 8 weeks given at the age of 7 or 8. Heller and Rogers have for some time advocated doses of 4,000 units 3 times a week up to 40,000 which can be given safely at any age and repeated if deemed advisable.

Since all testes do not respond to the same dose of hormone and since standard dosages have not been established, one should administer an amount sufficient to produce recognizable changes in the external genitalia before assuming that a testis capable of descent is mechanically obstructed. Because of its effect on genital tissue, chorionic gonadotrophin can also be well utilized after orchiopexy in patients exhibiting poor genital development. Such use in 1 of my patients gave good results.

Testosterone, by intramuscular injection and buccal absorption, has been effective in maintaining 4 of my patients who had androgen failure as a result of agenesis or atrophy. Smith observed that replacement therapy increased spermatogenic activity in eunuchoidism.

Factors in evaluation of the patient. Evaluation should include questioning the patient as to whether the testis involved has ever been in the scrotum.

Inspection of the patient before palpation is attempted often gives valuable information. It may immediately reveal the position of the testis. It will show if the scrotum is undeveloped, in which event the testis has likely never resided there.

When examination does not reveal the testis, I find it helpful to initiate the cremaster reflex and watch the response carefully. Often with the contraction of the cremaster muscle the position of the testis is indicated by a slight wavelike motion of the overlying skin.

The ease and the accuracy of palpation depend to a large extent on the age of the patient and the amount of fatty deposit in the puberal area. The obese child may present a difficult problem and require several examinations before diagnosis can be established.

To minimize errors, palpation should be done with the patient in both the supine and the standing positions. Bimanual examination is desirable, particularly in determining if the testis is movable; the extent of its mobility which is limited by the confines of the bursa; and if it can be manipulated into the scrotum or if it deviates to one side (fig. 12). Browne and also Corbett considered manipulation of the testis laterally important in differentiating the testis arrested in the normal line of descent from the one in the superficial inguinal pouch.

By having the patient cough or strain it is often possible to differentiate the testis temporarily arrested in the canal from the one fixed in this position. This procedure will also establish the presence or absence of a clinical hernia.

During the examination it is also important to look for pubic hair, especially in the boy approaching puberty. Its presence is the earliest clinical evidence of beginning maturity. Often the patient presents, or gives a history of, gynecomastia. At puberty it indicates an imbalance between androgens and estrogens (Nyda).

Factors in choice of treatment. In the absence of complications, such as hernia, torsion and arrest in an ectopic position, all of which demand surgical intervention, the age of the patient and whether he has bilateral or unilateral retention are the most important factors to consider.

Adults usually come in because of a complication, as was demonstrated in this

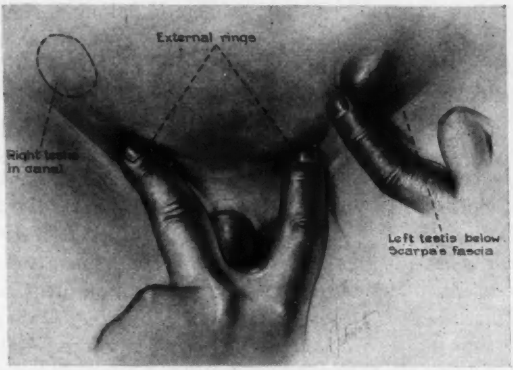

FIG. 12. Manner of demonstrating testis in superficial inguinal pouch. This picture also shows the bilateral retention of 1 patient. While the canalicular testis could be palpated, manipulation did not increase its prominence. When the opposite testis was manipulated laterally it became more prominent.

series. During treatment of the complication the retention is also corrected, and at this age correction must usually be orchiectomy. The puberal boy with 2 undescended testes presents no problem because corrective measures are commonly instituted immediately. And treatment of the puberal boy with 1 undescended testis is probably not neglected now either. But treatment for the prepuberal boy with unilateral retention, and more particularly for the one with bilateral retention, has given rise to a controversy. The crux of the controversy centers around the best time for placement.

Some surgeons advocate orchiopexy in early childhood because of the changes Cooper and others have observed on histologic study of retained testes. Although they acknowledge the hazards attending operation in young children, in their opinions the retardation in development resulting from the retained position overshadows the possibility of delayed descent at or even after puberty.

Other surgeons defer orchiopexy until early puberty unless complications make operation necessary before this. While they do not minimize the accumulating histologic evidence of retarded development in the retained position, most of them take advantage of the latitude permitted by the considerable number of testes that come down at puberty. In following this course they expect the spontaneously descended testes to be better than those subjected to the trauma of operation. That testes descending late develop to complete maturity after reaching the scrotum is evidenced by paternity in 8 patients in this series.

Whether operation is done early or late, most surgeons now favor a preliminary trial of chorionic gonadotrophin to differentiate the testes that are likely to come down by themselves from those that have to be brought down surgically. It remains, therefore, to emphasize that administration of chorionic gonadotrophin should not be delayed beyond puberty when the re-awakening Leydig cells usher in the secondary male characteristics. I see no objection to the use of chorionic gonadotrophin as a diagnostic procedure in the prepuberal boy with

bilateral retention, particularly if the testes are impalpable. And I favor the use of 4,000 international units 3 times a week up to 40,000 units. With this dosage repetition of hormone administration has not been necessary in my patients in this series and those subsequently treated.

If the testes do not descend after adequate hormone therapy, orchiopexy should be done. But this should not be done later than puberty.

While the Keetley-Torek operation gives good results in many patients, its chief disadvantage is the possibility of excessive tension on the blood vessels of the cord. When the cord is of sufficient length to bring the testis to the bottom of the scrotum, I believe, with others, that a one-stage operation is preferable. If bilateral undescended testes cannot be brought to the bottom of the scrotum, they should be placed in a high scrotal position or in a position outside the external ring rather than removed. However, orchiectomy is advisable for the unilaterally retained testis that cannot be placed in the bottom of the scrotum. At no time should testes be placed in the abdomen where detection of early malignancy would not be possible.

In carrying out orchiopexy it is well to protect the ilio-inguinal nerve and to free the bursa completely from its attachments. This is done by severing the projection of external spermatic fascia which holds the bursa in the retained position. Traction on the severed fascia elevates the bursa and facilitates freeing it from the transversalis fascia posteriorly and its attachment to the internal oblique and transversus muscle laterally. Continuing the dissection cephalad allows freeing of the spermatic vessels well into the abdomen. I defer opening the bursa until this dissection has been completed. Stripping the processus vaginalis and the posterior peritoneum from the vessels permits high ligation of the processus vaginalis. Additional length may be gained by releasing any fibrous adhesions which may be causing adherence of the blood vessels.

If still more length is needed it can be obtained by incising the internal oblique laterally, as advocated by Wangensteen, or splitting the internal oblique, as suggested by Kiefer. While incision of the transversalis fascia and ligation of the inferior epigastric vessels will add length to the vas, I do not believe length of the spermatic vessels can be obtained in this manner. Because of this and because of the importance of the transversalis fascia in maintaining a strong abdominal wall, I have avoided incising it. However, if the extreme shortness of the vas left no alternative, I would incise the transversalis fascia and divide the epigastric vessels.

In anchoring the testis in the scrotum care must be taken not to obstruct the proximal vas which courses through the peritoneum just below the testis. I have found that the following procedure is satisfactory for anchoring the testis in the bottom of the scrotum:

Two catgut sutures are passed first through the dartos, then the visceral layer of the tunica vaginalis and the tunica albuginea. A third suture of silk, for traction, is placed in the bottom of the scrotum as near as possible to the septum and carried through the visceral layer of the tunica vaginalis and the tunica albuginea between the two previously placed catgut sutures. The traction suture is then

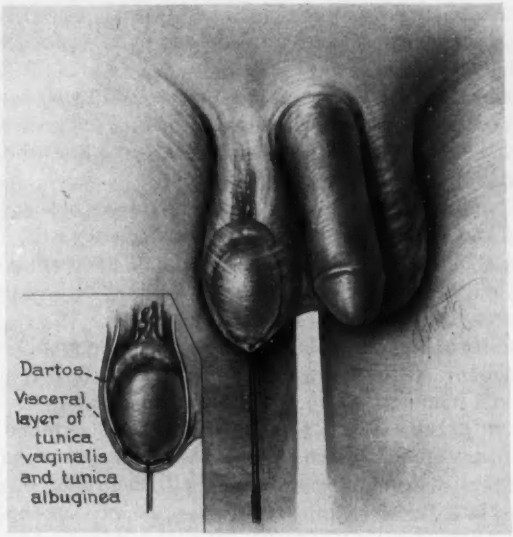

FIG. 13. Method of anchoring testis to dartos in one-stage orchiopexy. Note traction suture

tied to a rubber band which is secured by adhesive tape to the thigh on the side of the orchiopexy (fig. 13). At the end of a week the traction is removed.

In repair of the operative site the Ferguson procedure of not transplanting the cord has distinct advantage. Brought out of the wound lateral to the pubic tubercle, the cord lies in a direct line to the scrotum. All the length that has been obtained is thus preserved. However, with this procedure it is necessary to make sure that the inguinal canal is left as strong as possible. When the structures of the inguinal canal appear to be deficient, it is better to transplant the cord and use fascia in the repair instead of catgut.

SUMMARY

In this series orchiopexy was deferred until puberty unless complications demanded earlier intervention. It includes testes that came down without treatment as well as some that responded to hormone stimulation.

Of 153 patients in the series, all but 3 were traced, the longest followup period being 33 years. Of the patients traced, 49 had bilateral and 101 had unilateral retention, making a total of 199 testes.

Seven obese prepuberal and puberal boys have been aided in general development as well as genital growth by a regimen of diet, thyroid as indicated, and gonadotrophic hormone, which was given to 6 boys.

Four eunuchoid men are being maintained with testosterone by intramuscular injection and buccal absorption.

Eighty-six associated hernias were repaired, and torsion in 3 patients was corrected.

Delayed spontaneous descent occurred in 44 testes.

Exploration disclosed gross congenital defects in 17 testes (8.5 per cent). In 11 instances the defect was agenesis.

Orchiopexy was done for placement of 86 testes—59 by a one-stage and 27 by a two-stage procedure. Four testes required secondary orchiectomies.

Primary orchiectomy was carried out in 35 patients, 3 of whom were puberal boys and 32 adults.

Four adults having orchiectomy for malignancy have now been alive, respectively, 5, 6, 6½ and 15 years. The incidence of malignancy is 12.5 per cent on the basis of cancer in 28 scrotal testes seen here and 2.01 per cent on the basis of 199 clinically retained testes. When the 44 testes descending spontaneously are removed, the percentage is 2.76.

Biopsy of 4 testes at orchiopexy in puberal boys showed prepuberal tubules in 1. Germinal epithelium (spermatogonia) was preserved in 3. Biopsy of both testes at orchiopexy in a man aged 25 showed primary spermatocytes in both. This is the oldest patient in the series with preservation of the germinal epithelium.

Biopsy of 5 testes brought down by two-stage orchiopexies 4 to 10 years previously showed persistent prepuberal tubules in 3. Spermatogenesis was complete in 4 and arrested in 1. However, this was observed in only one-sixth of the tubules in the sections of each testis.

Microsections of extirpated testes in 3 puberal boys showed spermatogonia in 2 and Sertoli cells only in 1. Prepuberal tubules were preserved in all.

Microsections of extirpated testes in 22 adults, 18 to 73 years old, showed degeneration of germinal elements in all and preservation of Leydig cells in all but 3. Prepuberal tubules persisted in 5, indicating congenital defectiveness.

Cosmetic results were on the whole good. But the position, size and consistency of the testes were better after spontaneous descent than after either the one- or two-stage orchiopexies. Comparing the two types of orchiopexies, the position was better after the two-stage procedure, but the size and consistency were better after the one-stage operation.

Fertility was better after delayed spontaneous descent than after orchiopexy. Of 13 men who had bilateral delayed descent, 6 thus far are married and all 6 have fathered children. In 2 other men a testis that descended spontaneously on one side was responsible for paternity. Therefore, 8 men were fertile after spontaneous descent. Of 9 married men having bilateral orchiopexies, 4 have fathered children. Orchiopexy is credited with the fertility of 1 other man who had the operation at age 8 and spontaneous descent of the opposite atrophied testis at age 21. Thus, the paternity of 5 men can be attributed to orchiopexy which in each instance was a one-stage procedure which was done before puberty.

CONCLUSIONS

From the foregoing, the following conclusions have been reached:

The testes should be given an opportunity to descend spontaneously provided there are no complications such as hernia, torsion, or arrest in an ectopic position.

If descent has not occurred when the first pubic hairs appear and establish

beginning puberty, adequate hormone therapy should be instituted. If deemed advisable, hormone stimulation may be tried as a diagnostic procedure in the prepuberal boy with bilateral retention.

If adequate hormone stimulation does not bring the testes to the scrotum, it may be presumed that the continued retention is due either to mechanical factors or congenital defects in the testes. In either event exploration is indicated.

If testes are found they should be brought to the bottom of the scrotum by a one-stage procedure. If this is not possible, a high scrotal position or a position outside the external ring is preferable to orchiectomy in bilateral retention. But when the unilaterally retained testis cannot be brought to the bottom of the scrotum orchiectomy is advisable. No testis should be placed in the abdomen where detection of early malignancy would be impossible.

Neither hormone therapy nor orchiopexy should be delayed beyond puberty.

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THE EFFECT OF ACTH ADMINISTRATION ON THE URINARY EXCRETION OF ANDROGENS AND OTHER STEROIDS BY OLD MEN IN COMPARISON WITH YOUNG MEN: PRELIMINARY REPORT

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This is a progress report of a continuing study of the changes in endocrine status associated with increasing age in the adult human male. It is particularly hoped that studies of this nature may throw additional light on the etiology and rationale of therapy of cancer of the prostate and of the male breast. Previous publications from our laboratories[1–5] have reported the results of assays of the urinary steroids of patients with cancer of the prostate as affected by orchiectomy, adrenalectomy, and steroid therapy. In the present report, elderly men have been compared with young men, with respect to the effect of ACTH on the urinary excretion of 17-ketosteroids and 17-hydroxycorticoids, measured chemically, and of androgens measured by biological assay.

The decline in the urinary excretion of androgens and of total 17-ketosteroids with age has long been recognized. The pertinent literature has been reviewed by Dorfman,[6] Mason and Engstrom,[7] Hamilton[8] and Birke et al.[9] A study, recently reported by Dobriner,[10] in which the principal urinary steroids of 11 men under 50 and 9 men over 50 were individually quantitated, amply confirmed the earlier studies based on less discriminating methods. However, the excretion of urinary

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TABLE 1. *Comparative urinary excretion of 17-hydroxycorticoids, 17-ketosteroids, and androgens by young men and old men*

	17-Hydroxycorticoids (mg./24 hrs.)		17-Ketosteroids (mg./24 hrs.)		Androgens (I.U./24 hrs.) Mean
	Mean	Range	Mean	Range	
9 young men; age, 19–30.....	5	1–11	22	11–38	62
9 old men; age, 65–87.....	6	2–14	9	4–13	12

steroids known to originate exclusively from adrenal cortical precursors was not found to differ significantly between the two age groups. The question of possible differences in adrenal cortical activity related to age was re-examined in a subsequent study by Dobriner.[11] Here, no consistent differences in the effect of ACTH administration on urinary steroid patterns were found between two young men and two older men. The wide differences between individuals, however, suggested that it might be necessary to investigate the question more extensively, using larger numbers of subjects, and in the present report observations on nine subjects in each age group form the basis for our conclusions.

Extracts of acid-hydrolyzed urine were prepared and the 17-ketosteroids were determined by the method of Klendshoj et al.[12] and androgens by a modification of the baby chick comb weight method of Rakoff et al.,[13] previously described.[3, 14] 17-Hydroxycorticoids were determined by the method of Reddy et al.[15]

RESULTS AND DISCUSSION

The nine young men used in this study were 19 to 30 years of age. The nine older men were aged 65 to 87 years. Two of the older men had been orchiectomized, one for cancer of the prostate, and the other for bilateral epididymitis, but these deviations from normality were not reflected in detectable abnormalities of steroid excretion. All the subjects were in good health at the time of the urine collections.

The mean values and ranges for the urinary excretion of 17-hydroxycorticoids, 17-ketosteroids, and androgens during control periods are shown in table 1. In confirmation of other investigators, the excretion of 17-ketosteroids and androgens was found to be definitely lower in the older group, although there was a slight overlap. No significant difference in the excretion of 17-hydroxycorticoids between the two age groups was apparent, however.

The effect of ACTH administration on steroid excretion, as influenced by age, was determined in two separate studies. In the first experiment, the responses of

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TABLE 2. *Urinary excretion of 17-hydroxycorticoids, 17-ketosteroids, and androgens. Mean increase over control periods during 2-day period of administration of ACTH gel. Comparison of 5 old men with 5 young men*

	17-Hydroxycorticoids (mg./24 hrs.)		17-Ketosteroids (mg./24 hrs.)		Androgens (I.U./24 hrs.)	
	20 c.u.*	80 c.u.	20 c.u.	80 c.u.	20 c.u.	80 c.u.
5 young men; age, 20–30	8	20	6	19	no increase	28
5 old men; age, 65–87	9	32	2	20	no increase	12

* Daily dose of ACTH gel in clinical units.

TABLE 3. *Urinary excretion of 17-hydroxycorticoids, 17-ketosteroids, and androgens. Mean increase over control periods during 2-day period of administration of 25 U.S.P. units of ACTH by 8-hour intravenous infusion. Comparison of 4 old men with 4 young men*

	17-Hydroxy-corticoids (mg./24 hrs.)	17-Ketosteroids (mg./24 hrs.)	Androgens (I.U./24 hrs.)
4 young men; age 19–30	20	14	30
4 old men; age 65–76	10	11	8

5 young and 5 older men, all in possession of intact adrenals and testes, were compared. Control 24-hour urine specimens were collected on three consecutive days. ACTH in gelatin* was administered once daily for the 4 days immediately following, 20 clinical units on each of the first 2 days, and 80 clinical units for the final 2 days. The test was repeated on each man after an interval of two to three weeks. A summary of the results is shown in table 2. The rise in 17-ketosteroid excretion during ACTH administration was very similar in the two age groups, but, surprisingly enough, the rise in 17-hydroxycorticoid excretion by the older men was significantly greater than that of the young men, by statistical criteria. The rise in androgen excretion was detected only at the higher dosage level of ACTH, and was markedly greater in the young men than in the older men.

In the second experiment, 4 young men and 4 older men were administered ACTH† by 8-hour continuous intravenous infusion on two consecutive days. (Two of the older men had been orchiectomized, as noted above.) Control 24-hour urine collections were made for two to four consecutive days immediately preceding the administration of ACTH. The results are summarized in table 3. The results, with respect to the effect of age on the response to ACTH, were very similar to those of the first experiment, except in one particular, the smaller increase in excretion of 17-hydroxycorticoids by the older men as compared with that of the young men. The difference was statistically significant.

The effect of ACTH on the mean 17-hydroxycorticoid excretion by the young men was essentially the same in both experiments, in spite of the change in dosage, route and duration of administration, and nature of the ACTH preparation, the vagaries of the analytical procedure, and individual variation. The mean

* "HP Acthar gel," all of a single lot, supplied gratis by the Armour Laboratory.
† Corticotropin, supplied gratis from the Research Laboratories of the Upjohn Company.

response of the older men, however, was much lower in the second experiment, in which ACTH was administered by intravenous infusion. Before accepting this unexpected result as conclusive and attributing it to the nature of the ACTH treatment, however, we feel that additional studies will be necessary.

It has been demonstrated repeatedly that during ACTH administration the urinary excretion of 17-ketosteroids and 17-hydroxycorticoids increases markedly, and the data of the present report are in excellent agreement with studies by previous investigators. The increased excretion of androgens during ACTH administration, however, was first documented in recent preliminary reports from our laboratories,[2, 4, 5] and these earlier observations have now been confirmed and extended by the new data.

Furthermore, it has now been demonstrated that the increase in androgen excretion, in terms of international units per 24 hours, during ACTH administration, is much greater in young men than in elderly men. The percentage increase in androgen excretion during ACTH treatment over the control period was, nevertheless, greater in the older group. It is also of interest that the ratio of increase in androgens to increase in total 17-ketosteroids (I.U./mg.), was lower in the older group. It may be speculated that if ACTH administration were continued over a longer period of time, the androgen excretion of older men might approach that of young men.

In any event, these studies have demonstrated that older men can respond to ACTH administration by a considerably increased excretion of steroids, including androgens, although, with respect to androgens, perhaps not so promptly or vigorously as young men. The satisfactory explanation of differences in the excretion of 17-hydroxycorticoids between young and old men must await further investigation. Finally, it must be concluded that our data, thus far, are not in complete accord with the idea that the differences in adrenal steroid excretion between old men and young men are entirely the result of a decreased rate of secretion of ACTH in old men. The possibility remains that, in advanced age, the pattern of adrenal cortical secretion and the intermediary metabolic processes may also have undergone significant alteration.

LOCALIZED AMYLOIDOSIS OF THE URETER: REPORT OF A CASE

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Localized amyloidosis of the ureter is a rare condition. Lehmann[1] reported the first case in 1937, discovered at autopsy on a 67-year-old woman. In 1952, Gilbert and McDonald[2] reported the second case (the first in English literature), a 52-year-old white woman, on whom left nephrectomy was performed for hydronephrosis and left ureteral obstruction. In their case the lower calyx, inferior portion of the renal pelvis, and 3.0 cm. of the ureter were involved by amyloidosis.

We are reporting the third case of localized amyloidosis of the ureter.

CASE REPORT

A 71-year-old white woman, never in good health since the age of eleven, with a multitude of recurring allergic, gastrointestinal, circulatory, and other complaints, experienced a sudden high temperature, pyuria, and pain in the right lumbar region which responded poorly to antibiotic therapy. One such attack 3 months previously responded poorly to treatment. The history included a diagnosis of granulative urethritis 9 years ago, treated by urethral dilatations. A retrograde pyelogram at that time was not remarkable (fig. 1, *A*). Cystoscopic and radiographic studies demonstrated a normally functioning bladder and left kidney, and marked right hydronephrosis and hydroureter due to organic obstruction of the right ureter about 3 cm. from the bladder (fig. 1, *B*). A right nephroureterectomy was performed, followed by normal convalescence.

Pathological report: The gross specimen was a 13 by 9 by 4 cm. kidney with 20 cm. of ureter attached. The latter, averaging 1.5 cm. in diameter, was obstructed 2.0 cm. proximal to its surgical margin by a 2 by 1 by 1 cm. firm, tan mass that uniformly involved the ureteral wall. The dilated renal calyces and pelvis contained grossly purulent material.

Microscopic description: The ureteral mucosa was focally lined by transitional epithelium with scattered, shallow ulcerations. The propria was diffusely infiltrated by lymphocytes, plasma cells, macrophages with foamy cytoplasm, and scattered neutrophils. There were scattered foci of necrotic cellular debris. In the mucosal propria, and largely obliterating the muscularis, were sheets and ovoid deposits of palely eosinophilic, homogeneous material. These deposits occasionally lay beneath the endothelium of small blood vessels. Rare multinucleated giant cells bordered the deposits. See figure 2. Peripherally, lying within the adventitia, was a rim of irregular bone trabeculae with foci of osteoid tissue that occasionally lay immediately adjacent to, but appeared demarcated from, amyloid deposits (fig. 3). The bone trabeculae often encased fatty stroma, but marrow cells were not identified. Sheets of amyloid frequently lay within

[1] Lehmann, G.: Zentralbl. f. allg. Path. u. path. Anat., **68:** 209–213, 1937.
[2] Gilbert, L. W. and McDonald, J. R.: J. Urol., **68:** 137–139, 1952.

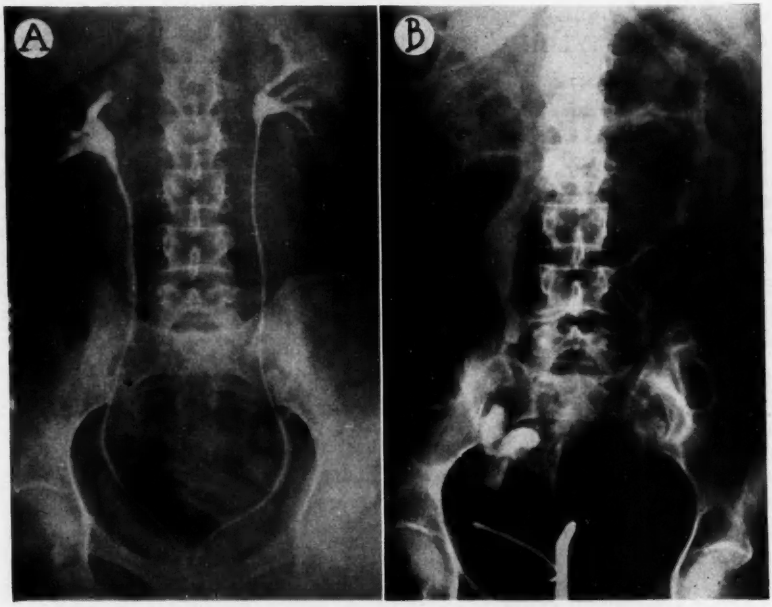

FIG. 1. *A*, retrograde pyelogram 1945. Essentially normal. *B*, retrograde pyelogram 1954. Tiny, hair-sized channel runs upward toward greatly dilated, tortuous lower right ureter, indicating annular constriction of lower ureter.

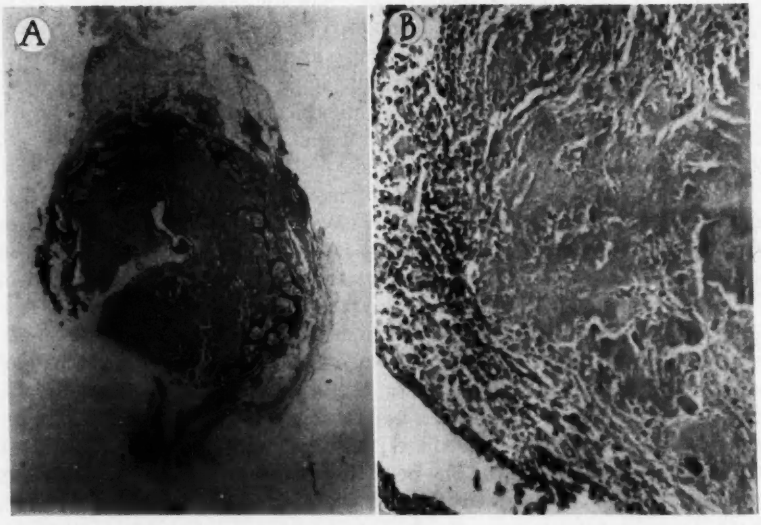

FIG. 2. Cross section of ureter showing a slit-like lumen, replacement of wall by amyloid, and peripherally located bone trabeculae. *B*, ureteral lumen at upper left, with underlying amyloid deposit.

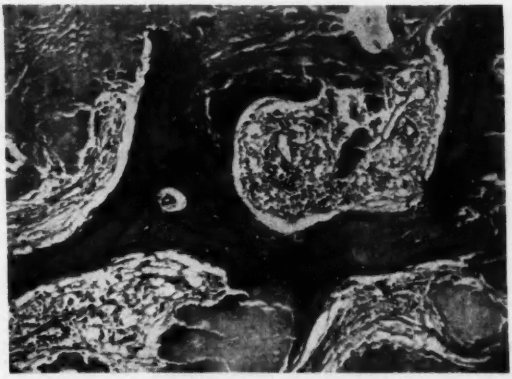

FIG. 3. Detail of bone formation with apposed amyloid deposits

these intertrabecular spaces, along with light infiltrations of lymphocytes and plasma cells. Rare osteoclasts were noted. In the adventitia homogeneous eosinophilic deposits occasionally bordered vessels, both subintimal and perivascular in location. With Congo red stain, these deposits appeared light orange to orange red. In a crystal violet stain they presented an uneven reddish purple hue.

Kidney sections exhibited focal interstitial infiltrations of lymphocytes, plasma cells and neutrophils in both cortex and medulla. Clusters of neutrophils lay within scattered tubule lumina. There was some clustering of glomeruli. The pelvic mucosa was focally ulcerated and heavily infiltrated by acute and chronic inflammatory cells. No acid-fast bacilli were seen in Ziehl-Neelsen stains of kidney and ureter.

Diagnosis: Localized amyloidosis, right ureter, with granulomatous inflammation and osseous metaplasia; hydronephrosis and subacute pyleonephritis, right.

Pre- and postoperative laboratory studies: Red blood cells, 4,200,000; hemoglobin, 12 gm.; white blood cells, 9,000. Differential: 6 stabs, 89 polys, 4 lymphs, 1 eosin. Blood Wassermann: Negative. X-rays of the chest and gastrointestinal tract were normal. A Congo red test revealed 30.4 per cent absorption of the dye, a normal result. Calcium, 9.2 mg. per cent; alkaline phosphatase, 2.5 units (Bodansky); total protein, 6.75 gm. per cent; albumin, 4.47 gm. per cent; globulin: 2.28 gm. per cent; A/G ratio, 1.96. The urine was negative for Bence-Jones protein. Bone marrow aspiration was refused.

DISCUSSION

The classification of amyloidosis as 1) secondary, 2) primary, 3) associated with multiple myeloma, and 4) localized, has been generally accepted. It is, however, of interest that in a recent report Wolf et al.[3] has questioned the validity of sharply segregating amyloidosis into distinct types. They reported a case of amyloidosis, unassociated with a predisposing disease, presenting features

[3] Wolf, R. L., Hitzig, W. M. and Otani, S.: A.M.A. Arch. Int. Med., **95**: 141–152, 1955.

of primary, secondary, and localized amyloidosis. However, to date in our case we have found no evidence of amyloid deposition other than in the ureter. The similarity of the clinical features of the case reported by Gilbert and McDonald and our own is striking, indicating the advisability of considering localized amyloidosis in the differential diagnosis of ureteral obstruction. Whether or not previous ureteral inflammation is a factor in the pathogenesis of this condition is uncertain. In our case there was history of previous urinary tract infection. Possibly the inflammatory reaction associated with the amyloid deposit was secondary. Bone formation, prominent in the ureteral adventitia of our case, is also described in Lehmann's report.

SUMMARY

A case of localized amyloidosis of the ureter with secondary hydroureter and hydronephrosis is reported. This is the third instance of this condition recorded in the medical literature.

DISCUSSION

DR. JOHN N. ROBINSON (New York, N. Y.): I should like to discuss Dr. Hand's paper and to congratulate him on a very comprehensive study of undescended testes. His results are extremely interesting, but I still would like to raise the old question, "How can we be sure that these testes which descend at the time of puberty or later show normal spermatogenic activity?"

I agree with Dr. Hand that it is important to replace a testis in its normal position as early as possible to give it every chance to develop normally and in order to prevent injury and to prevent cancer.

Dr. McDonald, in his paper, mentioned there was no stimulation of the testes from the use of cortisone under 5 years of age, which confirms our recent work and gives us the correct time to start treatment. I think 5 years of age or under is the best time. Most of these children are easy to handle; they respond well to injections of large doses of gonadotrophic substances given on three successive days. We have found that a certain per cent of these testes will come down normally in the scrotum within a week or ten days. The ones that do not come down have either very short cords, or congenital anomalies or are absent.

This slide shows the testis of a 28-week premature infant, and I think you can see the closely packed cells representing the tubule and the presence of Leydig cells.

This testis is normal.

Close observation of this next slide shows that there is very little difference between the two testes of this 5-year-old child. One testis was undescended and the other was normally descended in the scrotum at the time biopsies were taken.

These sections (slide) are of testes of a 10-year-old boy, and I don't think anybody needs to be told which side is normal and which side is undescended.

I feel very strongly that probably 25 to 30 per cent of these undescended testes are congenitally defective. We don't know which ones are congenitally defective, and which ones are not. In other words, if you have got a congenitally defective testis, I doubt very much whether it will ever develop; but we think these other testes, where there is some seminal insufficiency, will develop properly if put down in the scrotum as early as possible. Thank you.

DR. NORRIS J. HECKEL (Chicago, Ill.): I would like to say just a word about Dr. Higbee's paper. I must be very frank and admit that up until a few years ago amyloid disease of the genitourinary system, or amyloid disease in any part of the body meant to me that it was of interest only to the pathologist.

The disease was found very frequently in routine histological studies from the tissues of patients who were suffering from various wasting diseases such as tuberculosis, nutritional disturbances, cancer, and so on.

In our paper on amyloidosis of the genitourinary tract which was presented before the American Urological Association, a review of this subject was made and several patients with this condition were reported (J. Urol. **75:** 122–132, 1956).

Of particular interest was a woman who had intermittent attacks of hematuria which we thought at first from the cystoscopic picture were caused by endometriosis of the bladder, or a tumor located in the dome of the bladder.

She was admitted to the hospital and the lesion in the dome of the bladder was widely resected. (Slide) We were quite surprised when the pathologist reported the tumor to be amyloid.

Although this disease is rather rare in the genitourinary organ, it should be thought of in patients who have unexplained hematuria.

Just a word or two about Dr. Hand's paper and Dr. Robinson's discussion. It seemed to me that there was not a great deal of difference of opinion between them.

Strangely enough, there is still no unanimity of opinion among the profession on just how and when a child with an undescended testis should be treated. It seems to me that since the testis is supposed to be in the scrotum at the time of birth, the sooner it is placed in the scrotum after birth, the more likely will it be normal.

As John Robinson said, there are a certain percentage of these undescended testes that will never be normal, because they are defective in the first place. Our line of therapy is about as follows: Given a child with an undescended testis, we start him first on hormonal therapy.

We feel that this form of therapy will bring down those testes that would descend at or about the time of puberty (roughly 25 per cent). If after six or eight weeks of hormonal therapy with the gonadotrophins, the testis is not in the scrotum, we place it there by an orchiopexy.

Dr. Wyland F. Leadbetter (Boston, Mass.): I am very much interested in Dr. Hand's presentation, because it seems to me we have little evidence in the literature relative to the effectiveness of bringing testes down in the scrotum. I am not sure that I get from his paper whether he actually proves spermatogenesis in the testis that has been brought down at the time of puberty. I would like to ask him again if he has actual evidence of this.

Then there is something else that should be considered in regard to orchiopexy, namely, the operation itself. The purpose of bringing a testis into the scrotum, it seems to me, is to take advantage of the temperature-regulating mechanism which presumably is responsible for spermatogenesis. Theoretically, at least, for a testis to take proper advantage of the temperature differential, it should be at the extreme bottom of the scrotum to start with. In other words, if it isn't at the extreme bottom of the scrotum, I don't see how it can function effectively.

Orchiopexy is not purely a matter of getting the testis into the scrotum, we will say, if we are looking for spermatogenesis to occur.

I am not sure that anybody knows exactly what this temperature-regulating mechanism is. I don't know whether it is a function of cremaster ability to change the position of the testis, or whether it is dartos function. If it is partly cremaster function, I cannot see how the average orchiopexy is going to accomplish anything, because certainly there is no cremaster present when we bring a testis down in the usual fashion.

I am bringing up these points because it seems to me that what we ought to do in evaluating this problem is get down to the basic physiological principles that govern testis function.

I would certainly agree with Dr. Heckel that so far as I can see, the thing we want to do is to bring a testis down into the scrotum as early as possible, if we expect it to function normally.

DR. WILLIAM J. BAKER (Chicago, Ill.): I rise to ask a couple of questions. I would like to ask Dr. Heckel and Dr. McDonald whether they noticed any change in the size of the testes or the consistency of the testes in their series.

Secondly, we have an epidemic in Chicago, due to the influence of one teaching center, of routine orchiectomy for all undescended testes, and I am constantly besieged by pediatricians as to whether this should be done.

This teaching was brought about by the fact that a tumor of the testis occurred in a testis after it was brought down into the scrotum.

May I ask Dr. Hand whether he has ever seen a tumor of the testis develop in a testis after orchiopexy?

DR. REED NESBIT (Ann Arbor, Mich.): May I be so presumptuous as to answer for Dr. Hand one of the questions that Dr. Baker just proposed? It is too bad that Dr. Valk is unable to be at this meeting. He was expecting to be here, but was quite suddenly called home.

He told me only about a year ago of an instance of the type of case concerning which you have just inquired. A patient had undergone a Torek type of orchiopexy during early childhood. When Dr. Valk saw him, the man had a tumor in the testis which was at the bottom of the scrotum, having been placed there by means of the Torek type of orchiopexy.

Dr. Valk removed the tumor by an operation, and while the patient was on the operating table, Dr. Valk palpated his thigh and noticed that there was a a small area of induration at the site where the testis had been attached to the thigh when the patient had been subjected to the first stage Torek operation.

Thinking that this might be neoplasm, too, he excised the entire indurated area, and there was an identical tumor, where apparently some of the testis had been left embedded in the thigh.

There were no metastases in the abdomen, so that this secondary deposit probably was a second primary. That was, I think, an interesting case.

Recently I was privileged to see, at the North Central Section meeting, a splendid demonstration of a technique of orchiopexy by Dr. Prentiss of San Diego. It is one of the finest movies I have ever seen, incidentally.

In this procedure, Dr. Prentiss describes a new technique of orchiopexy, an adaptation of the Torek type of procedure, but he mobilizes the cord and cuts deep at the gastric vessels, so that he can remove the cord from the internal ring mesially, bringing it out directly through the external ring site. He has a nice diagram of geometry showing that what he accomplishes is an increase in the actual length of the cord by 24 or 26 per cent.

I performed this same operation about a month ago. I was doing an orchiopexy

and the cord didn't seem to be quite long enough to attach it to the thigh by the Torek technique, so I carefully measured upon the thigh the position of the testis when it was coming out in the usual place; then I carried out Prentiss's technique and moved the cord over laterally, went up retroperitoneally and did this whole technique that he so nicely described, but I didn't gain any lengthening of the cord. I wonder if any of you other gentlemen have carried out this particular procedure and could tell me whether your experience is different from mine.

Dr. Samuel A. Vest (Charlottesville, Va.): I would like to ask Dr. Harrison a question from his interesting data, in which he showed that androgens, i.e., the biological reactive androgens, have shown again a decrease in the aging male, at a time that the incidence of cancer rises.

Would this indicate that in all aging males going into the third decade of life, perhaps we should administer androgens and by this manner cut down on the high incidence of prostatic disease?

With regard to undescended testes, my endocrinological friends tell me that we, as urologists, should forget about the matter entirely, put aside all prior data, and begin all over again; that in the report of past cases we have not discriminated in doing the operation between testes in which there is no abnormality in the canal, which would probably descend later, and those in which there is an anatomical defect in the structures of the canal.

They say that in the first instance, there is a genetic defect which precludes spermatogenic function in later life. Both types of cases have been lumped together, and we need to do a careful examination of the individual patient to see whether the testes can be pushed down, or will descend without obstruction. I doubt that we, as urologists, have never brought any evidence that orchiopexy has produced function in those cases.

All of us know of sterility that we see in later life, in which biopsy of the testis showed various defects of the tubules, without explanation.

Maybe it goes back to the child. If we had a way of going over again cases that we see in our office and knew their history in their early life, whether they had late descent or not, it would be a very important piece of work. That certainly needs to be done.

Dr. Luis A. Sanjurjo (San Juan, Puerto Rico): In relation to Dr. Nesbit's discussion of the Prentiss technique, several years ago I had an opportunity to operate upon a 14-year-old boy with cryptorchidism on the left side. Upon opening the canal, we found he had a direct and indirect inguinal hernia, and of course I had to liberate both sacs, incise the floor of the inguinal canal, which is more or less like the Prentiss technique, but I couldn't bring that testicle down to the scrotum by any means and was faced with the problem of removing the testicle, which I finally did.

Dr. Rubin Flocks (Iowa City, Iowa): I wish to discuss first the operation for undescended testis. We have had relatively a small experience with this, but have felt that the more extensive mobilization of the cord structures stimulated primarily by the report of Dr. Prentiss has helped us in some instances. In other

instances it has made no difference in the length of the cord structures that we could determine.

I would like to also say one or two words with regard to Dr. Harrison's paper, which I think is very interesting, and I want to congratulate him upon his work in this regard, because I know from my own experience how extremely time-consuming and difficult it is to make these determinations.

We have been working along the same lines and have attempted to differentiate in the older group between those who have carcinoma and those who have not developed carcinoma. I am wondering whether he has found any difference in response to the ACTH in these older individuals who have carcinoma as contrasted to the ones who have not. Thank you.

DR. JAMES H. MCDONALD (Chicago, Ill.): In answer to Dr. Baker's question, examination of the testes during and after treatment with cortisone didn't reveal any particular change in either size or consistency.

DR. J. HARTWELL HARRISON (Boston, Mass.): (Closing) First I would like to thank Dr. Herbst for his continued interest in our investigations through the years, and for the inspiration which his own work has furnished to us.

We have not done any enzyme studies in this investigation. Unfortunately, the complexities are such that we necessarily have had to be confined to steroidal and biological androgen studies. Our laboratories are now able to do estrogen determinations by biologic measurement and we have reported previously our studies with reference to FSH. I should have mentioned during my talk that the results of our studies in comparison of young and old with reference to FSH have been somewhat different from those that Dr. Valk has obtained. We find that the mean average of FSH excretion in those between the ages of 20 and 30 ranges between 20 to 25 mouse units. In the older age group, 65 to 85 years, we found FSH is definitely elevated, being close to a mean of 65 mouse units. Dr. Valk's figures are lower than these and we will have to compare our laboratory methods and standards.

Dr. Vest's question demands a little philosophic dissertation, I believe. One sees life biologically as a continual process of growth in which cell multiplication and division occurs in a normal purposeful manner, which progresses in well-controlled patterns. The control seems to be the endocrinologic balance of the pituitary and its dependents. When organs lose their purposeful function, as do the prostate and the female breasts, then abnormal growth seems to begin. This implies that there is some reciprocal control between normal function and normal growth, and that perhaps loss of function may result in abnormal growth. Unfortunately, the administration of androgens to the middle aged or elderly male does not restore normal function and I believe will not necessarily prevent abnormal growth. Dr. Vest always asks penetrating questions and one cannot give a didactic answer to this question.

Dr. Flocks' question, regarding the difference between the elderly patient without cancer and the elderly patient with cancer, is closely related to the above by implication. We do have some figures on this problem:

In a group of five elderly men without cancer we found a mean of 15 inter-

national units of androgen measured biologically, and in a larger group of men with prostatic cancer, there was a mean of 11.8 international units excreted in 24 hours. It seems that on the basis of a percentile estimate that this would be a significant difference. However, this must undergo statistical analysis.

The fact that hyperplasia and cancer of the prostate each occurs when gonadal function is diminished is a challenge to detect the result of such changes upon the organism as a whole. It is significant, as shown in this study, that with aging the potential of the adrenal cortex to produce androgens is diminished in the resting state and with stress. The dramatic inhibition of the growth of prostatic cancer by castration when gonadal function has already been spontaneously greatly diminished enhances the significance of the relatively small quantitative changes in androgens so produced.

We have not observed the occurrence of carcinoma of the prostate following administration of large doses of androgen. For example, a dynamic professor of anthropology has been administering to himself 100 mg. of testosterone propionate daily now for 10 years. We have been watching him with great interest and very careful palpation. Repeated cytologic studies of the prostatic secretion have been carried out, as well as serum acid phosphatase determinations. These have all remained within normal limits.

Our study would ideally be a longitudinal one following men from the age of 20 through the age of 80 years. Perhaps Dr. Rubin Flocks will be able to do this, but I am certain that I shall not be around to complete such a study.

We necessarily have had to fall back on a cross sectional study and therefore have presented you with the mean averages of these efforts. We are not prepared to recommend administration of testosterone propionate to men because of the attainment of an arbitrary age when gonadal and other hormonal functions are expected to fail.

Dr. John R. Hand (Portland, Oregon): I wish to thank the discussants for their remarks. In his excellent microsections comparing the normal and retained testes, Dr. Robinson has highlighted the retarded growth that occurs in retained testes after the age of five.

What the final answer will be regarding the best time for orchiopexy is difficult to predict. Biopsies before and after orchiopexy, examination of the ejaculate of men subjected to the operation, gonadotrophic surveys, and evaluation of fertility performance may be expected to bring us closer to the solution.

Dr. Leadbetter asked about the status of the testis at puberty. That is a very important question. The answer I have would be this: I have biopsy studies on 4 patients who had orchiopexies at puberty four to ten years previously. Microsections of all these patients showed spermatogenesis which was, however, limited to approximately one-sixth of the tubules present in each section. I also have 4 patients who had one-stage orchiopexies at puberty and who subsequently married and had children. This is positive proof that complete spermatogenesis is possible in testes retained until puberty. Six additional patients with spontaneous descent of both testes at puberty fathered children.

Dr. Baker asked about cancer of the testis following orchiopexy. I do not have a patient in whom a tumor developed in a testis that had been brought down, but I do have 4 patients with cancer of the testis in this series of 150 patients traced, or 2.01 per cent of the 199 testes involved. If I were to take away the 44 testes that descended spontaneously, the incidence would be somewhat higher.

Dr. Vest raised the question about sterility. The enlarged hard testis of a newborn infant recently subjected to exploration showed disruption of the entire testicular architecture by hemorrhage. This same process occurring below the level of clinical recognition in normal as well as retained testes may well be a factor in sterility.

Dr. Daniel R. Higbee (Denver, Colo.): I wish to thank Dr. Heckel for his discussion.

The pathologists are going to help us discover more of these so-called rare lesions, since they as a group are doing better work, on the average, than previously.

We don't want to overwhelm Dr. Baker with the large numbers of carcinoma of the testis which we as a group report, but I am sure Dr. Rusche will remember a pilot on the "Coral Sea" on whom I had brought down an undescended testis while he was in high school, because he couldn't run the 100-yard dash in less than ten seconds, and he thought placing the testicle in the scrotum would help him. Later on, carcinoma of the testis developed and eventually the patient died from it.

THE DIAGNOSIS OF TUMORS OF THE RENAL PELVIS AND URETER

VINCENT J. O'CONOR

In recent years, there has been a marked increase in the incidence of tumors arising primarily in the renal pelvis and ureter. There is sufficient evidence to prove that this recognition has not been due entirely to improved, or more universally applied, diagnostic procedures.

Just as the geographic incidence of papillary tumors of the bladder has followed the aniline-dye industry around the world, so also the increased finding of similar tumors arising in renal pelvis and ureter suggests a more common exposure to some sort of urinary carcinogen encountered in the daily routine of our present life. The occupational hazard of exposure to the aniline-dyes and various other petroleum derivatives is well recognized and is universally accepted as one of the two known specific causes of transitional-celled tumors of the urinary bladder. The other known specific etiologic agent in the production of bladder neoplasm is infection with Bilharzia (schistosomiasis).

During the past few years a number of carefully-controlled research projects in the dog, conducted separately in several English and American clinics, have conclusively demonstrated the carcinogenic effects of B-naphthylamine and allied products in the production of bladder tumors of a papillary nature. These excellent investigations have further shown that these carcinogens, if we may use that term loosely, are specific for the transitional-celled lining of the urinary tract and require, in addition to direct contact, something of a time element in this actual apposition to the mucosa. Lack of development of tumor in any portion of the bladder which has been marsupialized or removed from contact with the urine; development of tumors in the ureter or renal pelvis of the dog only after partial obstruction to the ureter has resulted in the urinary stagnation associated with hydroureter and hydronephrosis.

Therefore, the most important point in considering the subject of the diagnosis of tumors of the renal pelvis and ureter is the necessity to realize the relative frequency with which they may be encountered. Those of us who have been especially concerned with lesions of the urinary tract over a period of many years have probably learned this fact the "hard" way. As a result of our considering these tumors to be rare, stones have been removed from the ureter and renal pelvis without recognizing the fact that they were associated with small primary neoplasms. Many hydro- or pyonephrotic kidneys have been removed with portions of the ureter which were above the point of obstruction due to the primary ureteral tumor.

During my period of training at the Peter Bent Brigham Hospital, we encountered two instances of primary tumor of the renal pelvis and one tumor arising in the lower left ureter. This latter was considered unusual enough to form the basis of a report before this society by William C. Quinby in 1922.

In pursuing my interest in the subject of primary tumor of the ureter some years ago, I recall a statement made by someone to the effect that in the first

one hundred years of operation of the Massachusetts General Hospital only one instance of primary neoplasm of the ureter was recorded. Compare this incidence to the fact that some 20 years ago a urologist from a relatively small clinic in Wisconsin reported eight authentic cases in which a preoperative diagnosis had been made.

Since my assignment in this symposium limits my discussion to "diagnosis," I can best be brief and mention only the points which our own experience seems to emphasize as important.

Since July 1, 1942, on our service at the Chicago Wesley Memorial Hospital in Chicago, we have found 33 instances of primary tumor of the renal pelvis. Twenty-eight of these tumors were papillary (transitional-celled) in type and five were "solid" (squamous-celled). In the papillary tumors, eight had neoplastic involvement of the ureter also. Nine had papillary tumors of the bladder discovered at the original examination. Two other patients, upon whom nephroureterectomy was performed, were subsequently found to have tumors in the bladder. Thirteen primary tumors of the ureter, without evidence of renal involvement, were found. Eight patients with "ureteral stump" tumor involvement after nephrectomy were encountered. Seven of these had been nephrectomized elsewhere. In six of these patients, the data we could obtain seemed to indicate that no primary growth had been found in the removed kidney. A patient of our own, seen as recently as 1952, at which time I removed a large hydronephrotic kidney, returned in 1954 with gross hemorrhage from the ureteral stump. Excision of the ureter disclosed the presence of multiple low-grade papillary tumors which had undoubtedly been present as the cause of obstruction at the time of the original operation. Up to this date, there has been no bladder involvement in this patient.

Five of these 21 "primary" tumors of the ureter were flat, infiltrating squamous-celled growths. All had produced marked hydronephrosis with secondary infection in the ureter and kidney. These tumors spread early and all were found to have regional or distant deposits. The true nature of the "solid" tumor of the ureter is more difficult to diagnose preoperatively than is the case with papillary tumors. The lesions to be confused with primary tumors of the renal pelvis and ureter are those which cause mechanical obstruction, calculus formation, infection and gross hematuria; in other words, almost all the pathologic conditions which can arise in these structures.

Every patient presenting himself with papillary tumors of the bladder should be suspected of a similar type of lesion in one or the other urinary tree. Cystoscopic examination may show tumor projecting from the ureteral orifice as it did in eight of our patients. Radiographic study of the outline of the renal pelvis and ureter is, of course, necessary to arrive at a presumptive or positive diagnosis. The filling defect due to tongue-like protrusions of clear-celled carcinoma of the kidney into the renal pelvis has prompted a diagnosis of primary pelvic tumor on several occasions. Fresh or organized blood clots, "soft" or nonopaque calculi and necrotic renal papillae may provide pyelographic data simulating tumor of the renal pelvis. Wherever possible, attempts to outline the entire

ureter in case of extensive hydronephrosis may show a filling defect which would otherwise have been overlooked. If one is unable to outline the ureter and renal pelvis by excretory urography, and at the same time a catheter cannot be passed, it will be impossible to make a preoperative diagnosis. The only exception to this will be the finding of tumor cells in the urine, in which case it may be presumed that they have come from the obstructed ureter or renal pelvis. Up to now, these tests have not been helpful to us, but increasing technical skill in the future may prove such a search more worthwhile.

CONCLUSION

There seems to be definite evidence to prove that tumors of the renal pelvis and ureter are occurring more commonly than in the past. This trend will only be reversed when we identify the carcinogen, which we presume to be present in the urine. We will then take steps to eliminate or neutralize it. All patients with papillary tumors of the bladder should be suspected of upper tract involvement also, even though the percentage of positive findings will be small.

Modern diagnostic measures, plus a recognition of the possibility that neoplastic lesions may suggest stricture, stone, blood clots or other necrotic tissue will lead to a more ready recognition of the true condition.

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PATHOLOGY OF TUMORS OF THE RENAL PELVIS AND URETER

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AND

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In considering the pathology of tumors of the renal pelvis and ureter, one immediately ponders the problem of etiology. Perusal of this line of thought leads one into the multiple ramifications of conflicting views and terminology. An endeavor to reassemble these thoughts in some order of sequence necessitates the acceptance of certain fundamental facts and concepts.

EMBRYOLOGY

A study of the embryological origin of the kidney, ureter and bladder sheds some light on the pathology of tumors in these organs. For the embryology, Arey has been consulted, and is quoted freely without endeavoring to credit exactly individual sentences or words.

In the human embryo, the kidney develops in 3 stages. The first stage is the *pronephros*, which is a provisional, but functionless kidney.

The second stage of development is the formation of the *mesonephros* or wolffian body which is called the "middle kidney" since it is located more caudally. The tubules from the mesonephros drain into the pronephric duct (which was retained), but now becomes known as the mesonephric or wolffian duct. The mesonephros acts as a temporary excretory organ.

The third stage of development is the formation of the *metanephros* or permanent kidney. As in the case of the mesonephros, the metanephros consists of an aggregate of tubules which drain into a common duct. Here, however, the secretory unit or nephron (including Bowman's capsule, proximal and distal convoluted tubule, and Henle's loop) is formed from the caudal end of the *nephrogenic cord* (i.e., has an origin similar to that of the entire mesonephric tubule). The inert portion of the drainage ducts (ureter, pelvis, calyces, papillary ducts and straight collecting tubules) is derived from a bed growing from the mesonephric duct. The secreting tubule and the collecting tubule then unite to form a continuous *uriniferous tubule*. In structure and function these two components remain as different as was their origin.

The mesonephric duct makes a sharp bend just before entering the cloaca. It is at this site that the *ureteric bud* develops. The proximal part of the bud elongates to form the future ureter and the distal part forms the *renal pelvis* which pushes its way into the metanephrogenic mass above (which is the caudalmost portion of the nephrogenic cord). This mass promptly separates, and surrounds the pelvis, to become the permanent kidney.

The epithelium of the collecting tubules in the metanephros (which were derived from the nephrogenic cord) develops a tall columnar type of epithelium. The epithelium of the calyces, pelvis, and ureter (developed from the meso-

nephric duct), on the other hand, form a stratified epithelium known as a *transitional epithelium*.

In vertebrates below the placental mammals, fecal, urinary, and reproductive products all pass into a common entodermal chamber. Higher mammals (man) have subdivided this cloaca into a dorsal rectum, and a ventral bladder, urethra and urogenital sinus. Two separate outlets were formed, one for urine and the other for fecal discharge.

When the bladder finally emerges as a separate entity, it still receives on each side the common stem of a mesonephric duct and ureter. Growth processes quickly lead to the absorption of the common stems, resulting in 4 ducts with separate openings. By further shifting, the mesonephric ducts open at an elevation on the future urethra (known as Müller's tubercle). The two ureters come to lie well apart from each other at the superior corners of the triangular area (trigone). Temporarily this triangular area is an island of mesodermal epithelium amid the general entodermal lining of the bladder. However, it is soon replaced by encroaching sinus epithelium, so that the trigone is finally entodermal also. The general organization of the bladder with the formation of its stratified epithelial lining (transitional epithelium), is attained during the third month of fetal life. Thus, early in embryonic life, the bladder, ureter, and renal pelvis are lined with identical and continuous epithelium which is transitional in type. This explains why tumors arising in any of these three areas are similar in type and may be identical in histological appearance.

ETIOLOGY

The epithelium of the urinary bladder, ureter and renal pelvis is identical, and is called transitional in type. It varies from 1 to 6 cell layers in thickness. The superficial layers are constantly being cast off, to be replaced by newly formed cells from the deeper staining basal layer.

A cross section of a ureter (fig. 1) consists from the inside out of:

1) Mucosa—a lining layer of transitional epithelium which may be from 1 to

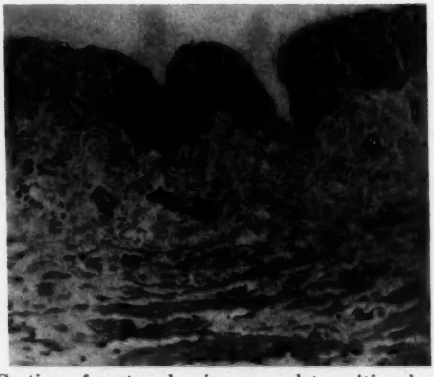

FIG. 1. Section of ureter showing normal transitional epithelium

6 layers deep. The basement membrane is not distinct, and blends intimately with the connective tissue of the tunica propria.

2) Tunica propria—composed of dense connective tissue intermingled with elastic fibres. Occasionally it contains lymphnodules.

3) Muscle coats—3 more or less distinct layers: inner, longitudinal, middle circular, and outer longitudinal.

4) Tunica adventitia—which is loose fibrous connective tissue continuous with the exterior of the kidney above and with the exterior of the bladder below.

The changes which may occur in the epithelium are described below.

THE EFFECT OF CHRONIC IRRITATIVE CHANGES ON THE EPITHELIUM

A) Proliferative

B) Metaplasia

Chronic irritation may cause a proliferative form of pyelitis and ureteritis or epithelial metaplasia.

A) *Proliferative.* If the irritant causes a proliferation of connective tissue in the tunica propria so as to form granular or polypoid projections into the pelvis or ureter, the condition is referred to as: 1) ureteritis granulosa or pyelitis granulosa, and 2) ureteritis polyposa or pyelitis polyposa.

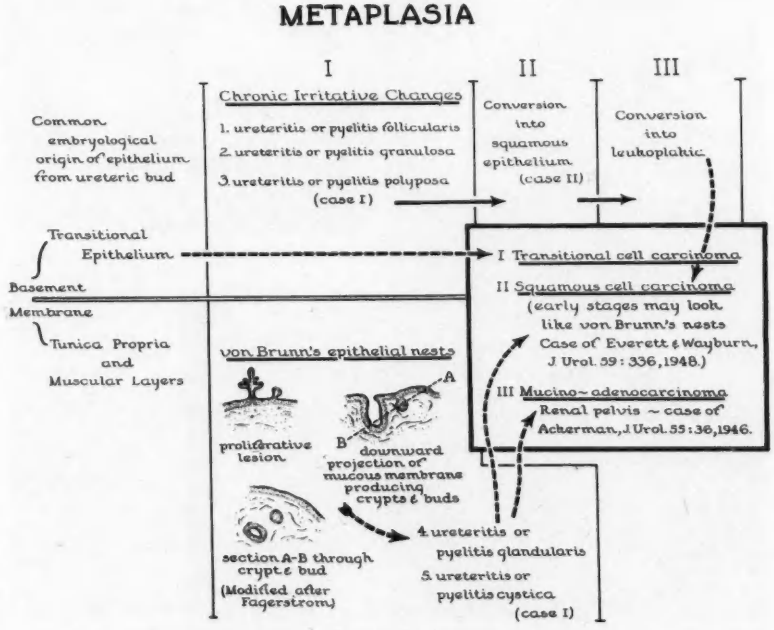
METAPLASIA
I
II
III
Chronic Irritative Changes
1. ureteritis or pyelitis follicularis
2. ureteritis or pyelitis granulosa
3. ureteritis or pyelitis polyposa (case I)
Conversion into squamous epithelium (case II)
Conversion into leukoplakic
Common embryological origin of epithelium from ureteric bud
Transitional Epithelium
Basement Membrane
Tunica Propria and Muscular Layers
I Transitional cell carcinoma
II Squamous cell carcinoma (early stages may look like von Brunn's nests Case of Everett & Wayburn, J Urol. 59: 336, 1948.)
III Mucino-adenocarcinoma Renal pelvis – case of Acherman, J Urol. 55: 36, 1946.
von Brunn's epithelial nests
A
B
proliferative lesion
downward projection of mucous membrane producing crypts & buds
section A-B through crypt & bud
(Modified after Fagerstrom)
4. ureteritis or pyelitis glandularis
5. ureteritis or pyelitis cystica (case I)

FIG. 2. Diagram showing changes of chronic irritation and metaplasia

When small lymph follicles are formed in the tunica propria, they also may elevate the epithelial lining; this change is called: 3) ureteritis follicularis or pyelitis follicularis.

If, however, the irritant causes a downward proliferation of epithelium into the tunica propria, there form solid nests of cells first described by von Brunn in 1893. These cell nests later develop a central cavity. The condition is then referred to as: 4) ureteritis cystica or pyelitis cystica. Many of these cysts contain fluid which gives a positive reaction for mucin (case 1, fig. 3). However, a lining

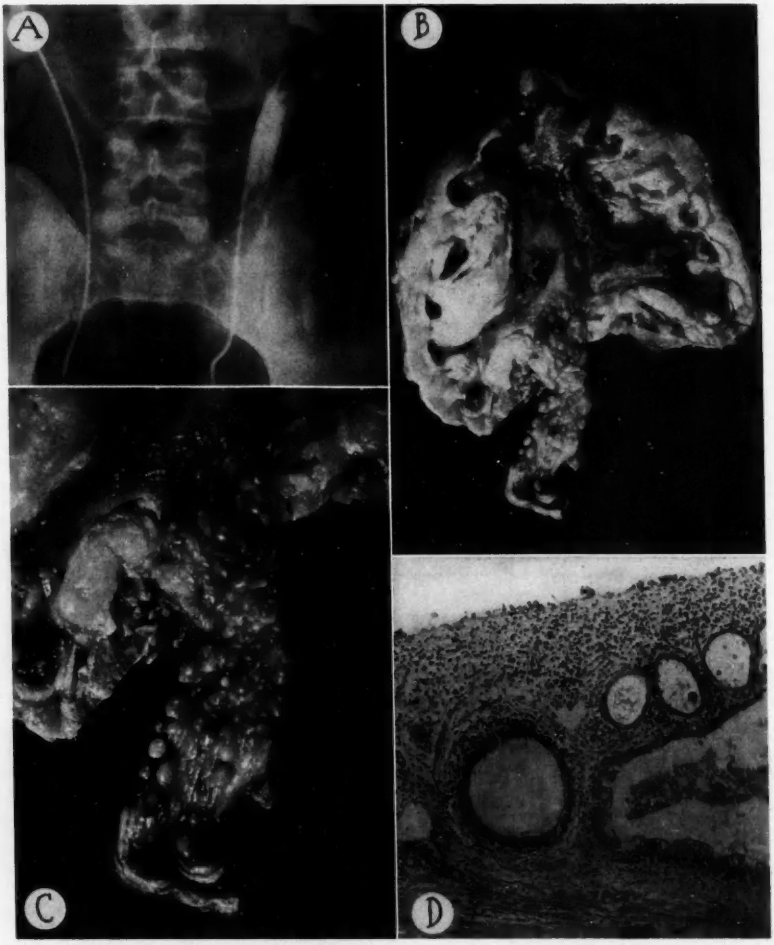

FIG. 3. Case 1. *A*, retrograde pyelogram showing typical filling defects in left ureter caused by cysts. Note partial staghorn calculus in left kidney. *B*, gross specimen showing staghorn calculus in situ, and grape-like cluster of cysts in ureter and pelvis. *C*, closeup view of gross specimen showing cysts. *D*, microscopic section of ureteritis cystica. (Reprinted by courtesy of British Journal of Urology; MacLean: Brit. J. Urol. **26**: 136, 1954.)

of typical goblet cells as occurs in mucinous metaplasia (or true pyelitis glandularis) is not present, and the overlying epithelium is transitional in type.

Stirling and Ash do not believe that the epithelial nests are the result of the downward proliferation of epithelium, but that they are the blind ends of mucosal crypts. They contend that if serial sections are properly cut through such an area, the alleged cell nest will always show a communication with the surface.

In Fagerstrom's detailed study of proliferation of tumors of the renal pelvis and ureter, it was not established that solid epithelial buds were the origin of solid tumors of the urinary tract. See figure 2.

B) *Metaplasia.* Epithelial metaplasia is the conversion of one type of epithelium to epithelium of another type.

1) Squamous metaplasia (changes to squamous cell epithelium): Prolonged irritation may lead to changes in the transitional epithelium which result in its conversion to a squamous cell epithelium characterized by thin platelike cells which are arranged in one or more layers that adhere to each other closely by their intercellular bridges. The cell layers eventually become more numerous with the formation of rete pegs and papillae. The squamous epithelium develops a line of keratinization, and there is desquamation of the surface cells into the lumen (case 2, fig. 4).

Leukoplakia by definition means "white plate." Keratin on the surface of squamous epithelium produces this white plate in the urinary tract. Although in some cases of squamous metaplasia, down growth and nuclear atypism may develop in the basal part, these changes are not necessary for the condition to be called leukoplakia. If atypical changes do develop, the lesion is only a step removed from malignancy.

2) Mucinous metaplasia: Here the lining is changed to a columnar epithelium containing goblet cells. With down growth of this epithelium, mucus secreting

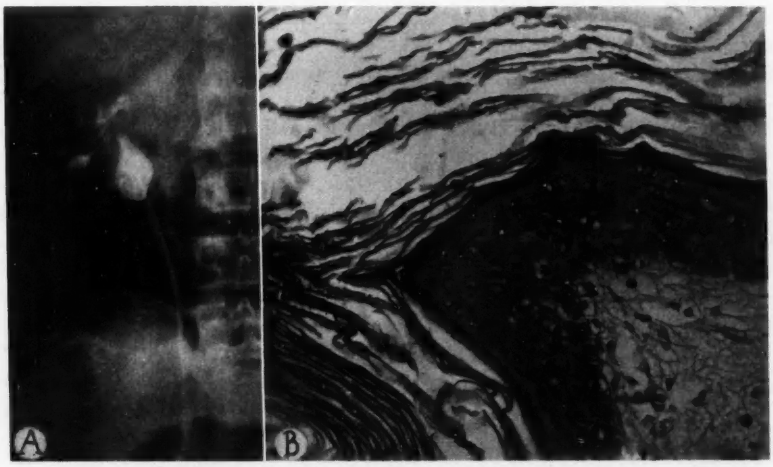

FIG. 4. Case 2. *A*, retrograde pyelogram showing filling defect in right renal pelvis. *B*, microscopic section showing squamous metaplasia of renal pelvis.

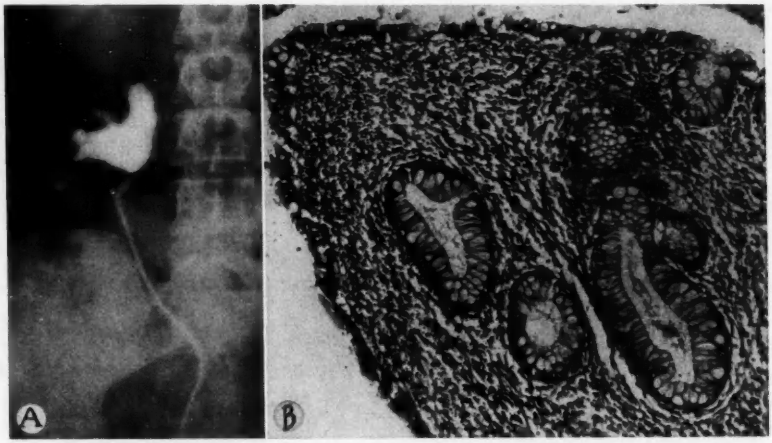

FIG. 5. Case 3. *A*, retrograde pyelogram showing staghorn calculus in right kidney and other calculi in lower pole. *B*, microscopic section showing mucinous metaplasia of renal pelvis. Note columnar epithelium lining pelvis containing goblet cells and formation of mucinous glands which extend into tunica propria.

glands are formed in the tunica propria. They are lined by goblet cells and resemble enteric glands.

However, metaplastic conversion of the transitional cell epithelium of the renal pelvis into the more specialized mucus-producing epithelium of the type that occurs in the colon is an exceedingly rare phenomenon, and mucous adenocarcinoma of the renal pelvis correspondingly rare (Allen). Up to 1950 only two cases of mucous adenocarcinoma of the renal pelvis had been reported (Ackerman; Ragins and Rolnick). A third case of mucinous metaplasia of the pelvis and part of ureter was recorded by Plunt. The authors wish to present a fourth case in which the renal pelvis only is involved. In this case it is evident that the condition is a true mucinous metaplasia (case 3, fig. 5).

The irritants which may produce the changes aforementioned are: 1) long continued bacterial infection; 2) obstructive uropathies; 3) presence of calculus; 4) avitaminosis, especially of vitamin A; 5) hormone imbalance; 6) toxic products of metabolism; 7) specific carcinogens.

Case 1 (fig. 3). Renal calculus, left; pyelitis cystica; ureteritis cystica; cystitis cystica.

N. S., a man aged 44, was admitted to Queen Mary Veterans Hospital December 19, 1946, because a routine urine analysis showed albumin, red blood cells, and white blood cells. He was entirely asymptomatic at this time.

Physical examination: Head and neck: entirely normal. Lungs: normal. Heart: not enlarged, no thrills, no murmurs, no irregularities; blood pressure 170/110. Abdomen: the liver was slightly palpable, but the spleen was not. Neither kidney was palpable. A left herniorrhaphy scar was noted. Locomotor system: entirely normal.

Laboratory investigation: Urine showed a specific gravity of 1.011; with 33 mg. per cent of albumin; sugar: negative; a few pus cells; red blood cells were not found in the urine at this time.

Blood count: The white blood cell count was 8,800; the bleeding time was 1 minute and the clotting time 13 minutes. Prothrombin time was normal. The platelet count was 260,000 per cubic millimeter.

An electrocardiogram was normal.

The blood nonprotein nitrogen was 20 mg. per cent.

Urinalysis done 4 days after admission showed 72 mg. per cent of albumin.

Excretory urography showed a partial staghorn calculus in the left kidney and filling defects in the left ureter, typical of ureteritis cystica. This was confirmed by retrograde pyelography at which time a differential phenolsulfonphthalein test was done. The dye appeared on the right side in 3½ minutes and on the left side in 6 minutes. Ten per cent of dye was collected on the right side and 4 per cent on the left side in 10 minutes. A 2-hour test showed 70 per cent excretion of dye.

On January 24, 1947, a left nephrectomy was done. Recovery was uneventful. The patient was discharged from the hospital 1 month later, after further followup investigation.

Pathological report: The left kidney weighed 198 gm. The surface of the kidney was smooth except for fetal lobulation. The pelvis and calyces were dilated and the pyramids were reduced in size. A large staghorn calculus occupied the greater part of the pelvis and extended into the calyces. Numerous small cysts were present on the mucosal surface of the pelvis and attached ureter.

Sections of ureter and pelvis showed edema and a moderate infiltrate of mononuclear inflammatory cells. Numerous cystic spaces lined by epithelial cells and filled with pink staining material were present in the tunica propria. There was dilation of the collecting tubules and an infiltrate of mononuclear cells in the medulla. Diagnosis: Nephrolithiasis; hydronephrosis and pyelitis and ureteritis cystica.

Case 2 (fig. 4). Change of transitional epithelium of renal pelvis to squamous cell type epithelium.

E. A., a man aged 42, was admitted to the Royal Victoria Hospital on July 6, 1954. He had been well up until one month prior to admission. At the time of admission he complained of severe right costovertebral angle pain, and pain in the right flank radiating down to the right inguinal region. The pain was made worse by walking, and somewhat relieved by lying down. At this time there was no gross hematuria, but the patient noted that he passed in his urine threads of white and red skin-like pieces. No burning on micturition and no polyuria were present.

Two days prior to admission, the patient experienced pain in his left elbow and left knee with definite swelling. The pain was severe, and was aggravated by movement. It was the first episode of such pain.

The patient gave a past history of having had a similar attack of pain in the right costovertebral angle, 20 years ago. At that time the pain radiated an-

teriorly downwards and medially to the abdomen and genitalia, and was associated with gross hematuria. He was treated symptomatically at that time, and the pain disappeared.

On physical examination, the temperature was 100F and the pulse was 100. Head and neck were entirely normal. Lungs normal. Heart: not enlarged to percussion, no thrills, no murmurs, no irregularities. Blood pressure 120/90. The abdomen was symmetrical and soft. The liver and spleen were not palpated. The kidneys were not palpable. There was tenderness in the right costovertebral angle, but nowhere else. Genitalia were normal. On rectal examination, the sphincter tone was normal. The prostate was slightly enlarged, but not nodular. Extremities: the left elbow was in a semiflexed position and painful to move. There was some swelling, no redness. The left knee was in a semiflexed position with swelling and fluctuation.

Laboratory findings: Urinalysis: acid, pH 5, specific gravity 1.015, albumin 2 plus, sugar negative; microscopic: 3 white blood cells per high powered field. Repeated urinalysis continued to show albumin. Blood nonprotein nitrogen was 41 mg. per cent. Uric acid was 9.2 mg. per cent. Blood count: hemoglobin 86 per cent; white blood cells 14,000; sedimentation rate 40.

Progress: On admission the patient was given hot compresses to the swollen joints, acetylsalicylic acid and codeine. In about a week, the pain in the joints subsided and the urological investigation was carried out. Excretory urography showed a normal left pyelogram; a deformity in the right renal pelvis was thought to be either tumor or nonopaque calculi. On two separate retrograde pyelograms, the filling defect in the right kidney continued. The diagnosis remained uncertain between nonopaque calculi and tumor.

On July 23, 1954, a right nephrectomy was done. Recovery was uneventful.

When the kidney was split open, it was found to be filled with debris present in layers, closely resembling the appearance of asbestos shale. There was no tumor present in the kidney. Subsequent sections of the kidney and renal pelvis showed that the transitional epithelium had changed to a squamous cell type of epithelium, and the shale found present in the pelvis was desquamated epithelium.

The patient was discharged from the hospital 13 days postoperatively and has remained well since.

Pathological report: The right kidney weighed 180 gm. Soft, friable, grey, flaky material resembling asbestos shale was present in the slightly dilated pelvis. The distal half of the pelvis was covered with a thin layer of greyish white material which extended to the ureteropelvic junction.

Microscopic sections showed the lining of the lower half of the pelvis to be composed of multiple layers of squamous epithelium with intercellular bridges and a distinct superficial granular layer. The surface was covered with a layer of keratin. The tunica propria throughout the pelvis was edematous and contained only a few lymphocytes and eosinophils.

The epithelium in the upper half of the pelvis was normal. A few scattered focal collections of lymphocytes were present in the renal parenchyma and a

few of the tubules contained casts. Diagnosis: Squamous metaplasia of renal pelvis (leukoplakia).

Case 3 (fig. 5). Renal calculus; pyelitis glandularis—mucinous metaplasia of pelvis; hydronephrosis and chronic pyelonephritis minimal.

S. E., a woman aged 39, was first admitted to Royal Victoria Hospital December 5, 1947, at which time she had a lump in her right breast. This was excised, and the sections showed that it was a fibroadenoma.

She then remained well until July 1949 at which time she was admitted complaining of low back pain of 3 months' duration, and cloudy urine with a very heavy sedimentation. The remainder of the history was normal except that she stated she occasionally passed some blood in the stool.

Subsequent investigation revealed two calculi in the right kidney and one small opacity in the region of the left kidney. The opacity present in the region of the left kidney appeared to be outside the urinary tract.

A barium enema showed a deformity in the region of the rectum suggestive of a carcinoma of the rectum. This was confirmed by sigmoidoscopic examination when the diagnosis of an anterior lesion of the rectum was made and biopsy proved it positive. This was followed by a combined abdominoperineal resection of the rectum with a permanent colostomy. The pathological report showed that the terminal 26 cm. of the rectum and sigmoid had been removed, including the anus and surrounding skin. On the anterior wall of the rectum, 4 cm. above the anorectal junction, a polypoid, firm, dark-red, ulcerated tumor measured 2.5 cm. in diameter and 1.5 cm. in height. Sections of the tumor showed it to be an adenocarcinoma of the rectum limited to the wall of the rectum. Recovery was uneventful and the patient was discharged from the hospital 18 days postoperatively. In August 1952 she was readmitted to the hospital on the urological service, at which time a staghorn calculus was found in the right kidney. A nephrectomy on the right side was advised, but refused.

She was readmitted to the urological service on March 28, 1955, because of recurrent attacks of cystitis, burning, frequency of micturition, and urgency.

On admission, physical examination: Head and neck were normal. Thorax symmetrical, movements equal and bilateral; lungs: normal percussion note throughout both lungs, breath sounds normal, no rales or crepitations heard. Heart: not enlarged, no thrills; there was a slight blowing murmur in the mitral area heard in late diastole. The blood pressure was 180/110. Abdomen: there was no tenderness in either costovertebral angle; neither kidney was palpable; the abdomen showed the colostomy stoma functioning well; the surrounding skin was well healed. No abnormal masses were palpated.

The pelvic examination revealed a normal uterus in normal position and a normal appearing cervix.

Special examinations: Urinalysis: acid, specific gravity 1.020, albumin 3 plus; microscopic: 40 pus cells per high powered field; occasional red blood cell and bacteria.

An electrocardiogram was essentially normal.

Hemogram: hemoglobin 90 per cent; red blood cells 4,500,000; white blood cells 8,300. There was no gross abnormal finding in the hemogram.

Blood Kahn negative. Blood nonprotein nitrogen 18.3 mg. per cent.

On April 1, 1955, a right nephrectomy was done.

Pathology report: The right kidney weighed 171 gm. The thin capsule stripped with some difficulty to reveal a pale external surface with scattered irregular, depressed scars. On section, the pelvis and calyces showed some dilatation and the distinction between cortex and medulla was lost in the scarred areas. The pelvis and calyces were thickened and their surfaces were granular. A few elevations measuring up to 3 mm. in diameter were noted. The 5 cm. of attached ureter had a similar appearance.

Sections of pelvis showed edema and a heavy infiltrate of lymphocytes and plasma cells in the tunica propria. Epithelial erosions were noted in multiple areas. In many areas the transitional epithelium was replaced by a layer of columnar epithelial cells, some of which contained droplets of mucus. In the tunica propria deep to this metaplastic epithelium were numerous mucus-secreting glands of the large bowel type. There was no evidence of malignancy. The kidney showed a few small focal areas of chronic pyelonephritis. There was a mild exudative inflammatory reaction of the tunica propria of the ureter but no metaplasia. Diagnosis: Renal calculus; pyelitis glandularis—mucinous metaplasia of pelvis; hydronephrosis and chronic pyelonephritis—minimal.

THE SIGNIFICANCE OF "PREDISPOSING FACTORS" AND OF SEEDING

The next important step is to recognize, as suggested by Ewing and by Waugh, that whatever the factors are that predispose to tumor formation in the urinary tract, there is no reason to believe that these factors are limited solely to the area in which the tumor occurs, but rather that the whole urinary epithelium is exposed to them. This may explain the presence of multiple papillary tumors in the renal pelvis and ureter. An alternative explanation is that "seeding" has occurred along the course of the ureter, from the parent growth above. Either view could be supported by the statement of Whitlock, et al., in which they state that of 33 cases of primary carcinoma of the ureter, there were 10 instances in which bladder tumors developed after removal of the primary carcinoma of the ureter.

The possibility of implantation by surface extension and spread along lymphatic channels is apparent.

The theory of the spread of tumor from the bladder into the ureter by reflux regurgitation up the ureter is singularly lacking in appeal.

THE CHEMICAL CARCINOGENS AND STEROIDS IN RELATION TO THE PRODUCTION OF CANCER

We are all familiar with the formation of bladder tumors in aniline dye workers, and of tumors of the scrotum in chimney sweepers. It is interesting to note that in 1775, Percival Pott, the distinguished British surgeon, was the first to suggest the idea of cancer being an occupational disease, due to a specific material, a constituent of tar.

This fact, and the subsequent progress of cancer research with its possible implications, are well described by Rhoads. In 1933 the British school of chemists led by Kennaway and his associates Cook, Dodds and Heiger succeeded in isolating from tar, the cancer producing substance which was named 1:2 benzyprene. The molecular configuration was established. Other compounds of a similar type were prepared synthetically.

Shortly after this, "the molecular composition of pure male and female hormones was described. It was obvious that the cancer-producing substance from tar and the steroid sex hormones had some similarity." "The chemical relationship between carcinogen and steroid hormone suggested, of course, the most important concept since the observation of Pott. This was that cancer in man may be due perhaps to a manufacturing mistake by the body in which there is formed a carcinogen instead of a natural hormone."

Scott and Boyd in 1953 added another brilliant chapter to our knowledge on the relationship between carcinogenic agents and the production of cancer. They were the first to produce experimentally early proliferative neoplastic lesions of the ureter and kidney pelvis, and primary carcinoma of the ureter using a known carcinogenic agent. They produced early proliferative neoplastic lesions after 32 months of beta-naphthylamine administration in a dog where stasis followed a right ureterosigmoidostomy. Carcinoma of the ureter was produced after 31 months' administration of the drug in animals where stasis had followed this implantation of the ureter into the isolated sigmoid bladder. They concluded that in addition to an unknown or known carcinogenic agent, urinary stasis might well be a contributing factor in the production of neoplastic lesions.

We have all pondered for some years the relationship between the excretion of steroids in the urine and the production of cancer. Cases have been reported in which bladder tumor apparently disappeared after the ureters were transplanted to the bowel.

INCIDENCE: AGE: DISTRIBUTION

Scott in his excellent chapter on tumors of the ureter in Campbell's *Urology* draws attention to the increasing frequency of reports on primary carcinoma of the ureter. Whitlock, et al., in reporting on 33 cases, state that there are now 312 reported cases of primary carcinoma of the ureter in the literature. Scott also notes that there have been 72 cases of primary benign tumors of the ureter recorded. The ratio of benign tumors of the ureter to malignant tumors is therefore approximately 1:4 (or 25 per cent benign).

From the years 1925 to 1954 inclusive, there have been 4 cases of primary carcinoma of the ureter operated on at the Royal Victoria Hospital. Of these 4 tumors, three were papillary infiltrating transitional cell carcinoma grade 2, one was papillary noninfiltrating transitional cell carcinoma grade 1. During the period 1932 to 1954 inclusive, there has been 1 case of primary carcinoma of the ureter found in 10,223 successive autopsies. In the period 1946 to 1954 inclusive, there have been 6 cases of primary carcinoma of the ureter operated on in the Veterans' Hospitals throughout Canada, and one case found at autopsy.

Age. In the benign tumors, the youngest reported is in a boy of 10, and the

oldest is in a patient age 78. In the malignant tumors, the youngest reported is age 22 in a female, and the oldest in a man of 89. The commonest age group for all types of tumors of the ureter, both benign and malignant, is that between 40 and 80 with approximately 60 per cent in the fifth and sixth decades of life.

Sex. Malignant tumors of the ureter may occur in either the male or the female with a slight preponderance of the reported cases in the male.

Location of growth. Approximately two-thirds of all the tumors of the ureter occur in the lower third. The remaining one-third of tumors are approximately evenly divided between the upper and middle thirds of the ureter.

TUMORS OF RENAL PELVIS

MacKenzie and Ratner, reporting on a case of tumor of the renal pelvis, stated that at the Royal Victoria Hospital from 1917 to 1931 inclusive, there were 96 cases of tumor of the kidney, only one which was a true growth of the renal pelvis. Since then, from the years 1932 to 1954, inclusive, there have been an additional 111 kidney tumors operated on at the Royal Victoria Hospital. Of these, 14 had primary carcinoma of the renal pelvis: 5 were papillary noninfiltrating grade 1; 1 was papillary noninfiltrating carcinoma grade 2; 5 were papillary infiltrating carcinoma grade 2; 1 was papillary infiltrating carcinoma grade 3; (6 noninfiltrating, and 6 infiltrating transitional cell carcinomas) and 2 were infiltrating squamous cell carcinoma.

In the Veterans Hospitals in Canada from 1946 to 1954 inclusive there have been 164 cases of primary kidney tumor either operated on, or found at autopsy. Of these 18 were carcinomas of the renal pelvis.

Thus in the total series of 471 cases of primary renal tumor, 33 were carcinomas of the renal pelvis giving an incidence of 7.0 per cent.

Multiplicity of tumors. Thomas and Regnier in 1924 in a review of the literature on tumors of the renal pelvis found an incidence of 23 per cent with multiple neoplasms in the ureter or bladder, or both, associated with tumor of the renal pelvis. Stricker in 1926 found that in 47 per cent of 175 cases of papillomatous neoplasms of the renal pelvis, neoplasm was also present in the ureter and the urinary bladder. Whitlock, McDonald and Cook, in reporting on 33 cases of primary carcinoma of the ureter, have made the significant observation that in 10 instances, carcinoma of the bladder developed after surgical removal of a primary carcinoma of the ureter and, in some cases, years afterwards.

Classification of tumors of the renal pelvis and ureter (fig. 6). The primary tumors of the renal pelvis and ureter may have an epithelial or mesenchymal origin. Tumors arising from epithelium are of the transitional cell type, squamous cell type, or adenocarcinoma.

The cells forming the transitional cell tumors resemble, more or less, the epithelial cells of the normal mucosa. These tumors are divided into three types: papillary noninfiltrating, papillary infiltrating, or nonpapillary infiltrating. The cells vary from well differentiated to anaplastic and markedly pleomorphic. There is frequently variation in a single tumor. The degree of differentiation is indicated by cell grading according to the method of Broders.

CLASSIFICATION OF TUMORS OF RENAL PELVIS & URETER

TISSUE OF ORIGIN

I Epithelial
- Gross: papillary 75 %; solid 25 %
- Microscopic (Whitlock, McDonald & Cook–1954)
  1. papillary carcinoma – grades 1,2,3
  2. papillary & infiltrating ca. – grades 2,3,4
  3. non-papillary infiltrating ca. – grades 2,3,4 (including transitional cell ca., squamous cell, & adenocarcinoma)

Note:
1. Structural type (i.e. papillary or non-papillary)
2. Presence or absence of infiltration
3. Cell type transitional or squamous
4. Degree of anaplasia

II Mesodermal
- Benign fibroepithelial polyp:
  myoma
  lipoma
  neurofibroma
  angioma
- Malignant:
  fibrosarcoma
  myosarcoma
  lymphoblastoma

III Endometriosis

IV Metastatic

FIG. 6. Diagram showing classification of tumors of renal pelvis and ureter

As Willis states, "Although it is customary, and for clinical purposes useful, to distinguish between benign papillomas and carcinomas of the urinary tract epithelium, it is impossible to make any real pathological distinction between them."

In the above classification of Whitlock, McDonald and Cook, so-called papillomas are listed as papillary noninfiltrating carcinoma grade 1. There are no infiltrating carcinomas with a cell grade of 1, and all grade 4 tumors are of the infiltrating type. The presence or absence of infiltration, and the degree of infiltration are of greater prognostic significance than the cell grade.

Typical invasive squamous cell carcinoma may occur in the pelvis or ureter and occasionally there may be islands of squamous cell carcinoma in the invading portion of a transitional cell carcinoma. The squamous cell carcinomas are histologically similar to those of the skin and are recognized by the presence of intercellular bridges and keratin or pearl formation.

Mucoid adenocarcinoma is extremely rare.

Although the mesenchymal tumors of the renal pelvis and ureter are rare, it is theoretically possible to have tumors arise from any of the tissues which form these structures. The majority of the fibromas are polypoidal tumors with a covering of transitional epithelium. Other tumors include myomas, fibromyomas, neurofibromas and hemangiomas. Of the malignant mesenchymal tumors, leiomyosarcoma, and lymphoblastomas, including Hodgkin's disease, have been described.

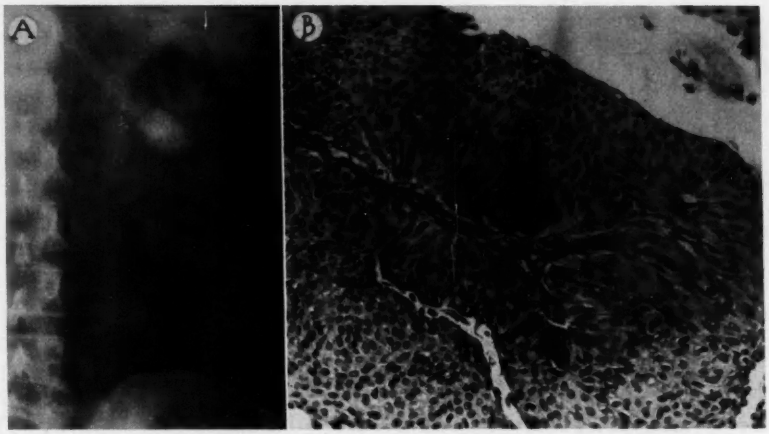

FIG. 7. Case 4. *A*, retrograde pyelogram showing deformity of left renal pelvis. *B*, microscopic section showing typical papillary transitional cell carcinoma in renal pelvis. Note thin central fibrous core, and mitotic figures.

Case 4 (fig. 7). Papillary infiltrating transitional cell carcinoma—grade 2—renal pelvis.

P. L., a man aged 61, was admitted to Ste. Anne's Military Hospital, March 2, 1945 complaining of intermittent hematuria over a period of 2 years, frequency and nocturia, day 8 to 10 times, night 4 to 5 times—of 3 days' duration; and suprapubic pain of 3 days' duration.

He gave a history of having had repeated attacks of gross hematuria while overseas during the past 2 years, but did not wish to report this to his medical officer for fear he would be sent home.

Physical examination: The patient weighed 267 pounds. His general appearance was excellent. The head and neck were normal. Lungs normal. Heart not enlarged; no thrills, no murmurs, no irregularities; blood pressure 140/85; abdomen: obese. There was slight tenderness in the left costovertebral angle. Neither kidney was palpated. The liver and spleen were not palpated. There were no abnormal masses palpated. The penis showed a first degree hypospadias, otherwise normal. Testes and epididymides normal. Rectal: sphincter tone normal. The prostate was enlarged about one and one half times normal size. It was fibroelastic, not fixed, not tender.

The urine was grossly bloody with scattered white blood cells in it. Nonprotein nitrogen 34 mg. per cent. Blood count: hemoglobin 95 per cent. Red blood cells 4,800,000. White blood cells 8,130. Phenolsulfonphthalein excretion test done after the gross hematuria cleared up showed a 2-hour excretion of 40 per cent.

Excretory urography showed a normal sized kidney on the right side with some enlargement of the kidney on the left side. The right pyelogram was entirely normal in appearance. The left pyelogram was irregular in contour with-

out any definition of the calyceal pattern in the upper pole and middle of the kidney.

Retrograde pyelography showed a normal pyelogram on the right with marked irregularity of the renal pelvis on the left with collections of dye in the upper pole and middle calyces of the kidney. This appearance was strongly suggestive of an intrapelvic tumor. Catheterized specimen from the right side showed a rare red blood cell and a rare white blood cell; on the left side there were 12 to 15 white blood cells and 1 to 2 red blood cells.

Twenty-four hour urine was examined for tuberculosis by smear, culture, and guinea pig inoculation. All reports were negative.

A diagnosis of tumor of the left renal pelvis was made. On March 19, 1945 a nephrectomy was done on the left side. Difficulty was encountered with the renal pedicle, as one vessel slipped out of the clamp. This was recovered, the bleeding was controlled. However, it was deemed inadvisable to carry out a dissection of the ureter at this time. The incision was therefore closed. Recovery was uneventful.

Pathological report: The left kidney weighed 280 gm. A large tumor with a rough, cauliflower-like surface filled the lower half of the pelvis and compressed and narrowed the parenchyma somewhat in this area.

Microscopic sections showed a papillary tumor with layers of cells covering thin connective tissue papillae. There was moderate cellular pleomorphism and occasional mitotic figures. There was superficial invasion of the wall of the pelvis. Diagnosis: Papillary infiltrating transitional cell carcinoma, grade 2; acute and chronic pyelonephritis.

Followup: The patient has remained well during the intervening 10 years. He was placed on a diet and reduced his weight to 195 pounds. His blood pressure remains at 140/85. Excretory urography done on January 24, 1955 showed normal function of the right kidney with an entirely normal pyelogram in which the major and minor calyces were clearly and delicately defined. The blood urea nitrogen is 22.9 mg. per cent.

Case 5 (fig. 8). Squamous cell carcinoma of renal pelvis.

J. B., a man aged 58, was admitted to the Royal Victoria Hospital January 10, 1944 complaining of gross blood in the urine, intermittently, for 1 year; pain in the right loin radiating to the back, for 1 month; frequency, nocturia and urgency, 2 weeks.

The past history was irrelevant to the problem concerned.

On physical examination, the eyes, ears, nose and throat were normal. The heart was not enlarged, there were no thrills, no murmurs, no irregularities. The blood pressure was 190/30. Lungs normal. Abdomen was obese; no tenderness and no masses were palpable. There was no costovertebral tenderness. Neither kidney could be palpated. On rectal examination the prostate was enlarged two to three times normal size. It was fibroelastic, not fixed, not tender and no nodules were palpated.

Laboratory investigation revealed that the specific gravity of the urine was 1.015; albumin 1 plus; sugar negative.

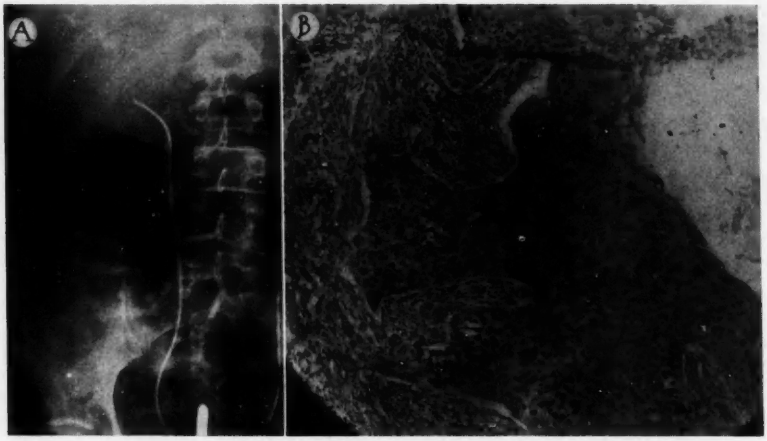

FIG. 8. Case 5. *A*, retrograde pyelogram showing filling defect in right kidney. *B*, microscopic section showing squamous cell carcinoma of renal pelvis.

The phenolsulfonphthalein excretion was 65 per cent in 2 hours.

Cystoscopy: With the patient under a low spinal anesthetic, the instrument was readily introduced. A large, black, ragged, oxalate stone, on the floor of the bladder, was found. Several growths were seen at the bladder neck, one in particular extending well into the right lobe of the prostate.

Under the same anesthetic, the bladder was opened, the stone removed, and a one-stage suprapubic prostatectomy performed. The prostate contained on its surface the tumor referred to at cystoscopic examination. The prostatic cavity was packed with an iodoform gauze and a Freyer tube inserted.

Pathological report: Sections of tissue from bladder neck showed a papillary tumor composed of delicate stalks of connective tissue covered by several layers of well differentiated epithelial cells. There were no mitotic figures or evidence of invasion. Diagnosis: Papillary transitional cell carcinoma grade 1 of urinary bladder.

Recovery was uneventful and the patient was discharged from the hospital 2 months after admission.

Progress report: Four months after the removal of the prostate and bladder tumor, cystoscopic examination failed to show any evidence of recurrence of bladder tumor. However, 2 months later, the patient was admitted to the hospital in an acute septic condition, complaining of pain in the right kidney region, intermittently, since his previous operation, plus an acute rise in body temperature of 1 week's duration with an increase of the pain in the right costovertebral angle.

Urine showed: albumin 1 plus, pus 4 plus; phenolsulfonphthalein excretion 40 per cent in 2 hours.

Cystoscopy showed a normal looking bladder with a white healed scar at the neck. Catheters were passed up each ureter, there was a good flow from the left,

but a poor flow from the right. The pyelogram on the left side was normal and the pyelogram on the right side was deformed, the lower calyces failing to fill, and the upper ureter being slightly dilated.

A diagnosis of tumor of the right kidney plus pyonephrosis was made and a nephrectomy was carried out on August 10, 1944.

The patient ran a very stormy postoperative course and finally died 3 weeks after operation.

Pathological report: The right kidney weighed 490 gm. The capsule was thickened and stripped with difficulty from a finely granular surface. Cut section showed the cortical and medullary markings to be somewhat obscured. The pelvis was all but obliterated by firm white tumor which extended from this region into the renal parenchyma and through the capsule at one point. Approximately one-third of the kidney was replaced by a tumor mass with an irregular margin.

Sections showed a squamous cell carcinoma arising in the pelvis and invading the medulla and cortex of the kidney. Keratinization was prominent in some areas. Diagnosis: Squamous cell carcinoma of renal pelvis.

Case 6 (fig. 9). Squamous cell carcinoma of renal pelvis containing glands and mucin-secreting cells.

M. C., a man aged 54, was admitted to Royal Victoria Hospital March 11, 1955, complaining of pain in the abdomen after meals for 1 year and also pain in the right hip for 1 year.

The patient was last perfectly well a year ago when he began to notice pain in the epigastrium spreading laterally, coming on approximately 1 hour after meals. It was described as a dull ache and was relieved partially by alkalies. Over the past 2 months his bowel movements had become harder and in smaller quantities than previously; this despite glycerine suppositories. On one occasion he passed a little blood following a particularly difficult movement. Fried foods, coffee and jam gave him an acid feeling in his mouth. He had lost 20 pounds over the past year. Barium enemas in September 1954 and February 1955 were normal. For approximately the same period of time he had had a steady dull ache in the sacral region, apparently brought on at work when he lifted a heavy box and slipped, thereby wrenching his back. There was no radiation and no change in the pain since the onset. He had pneumonia in 1903; a fractured arm in 1903; gasoline burns in 1947. The patient had had a productive cough for 15 years, worse in the past 6 months. The sputum was greenish in color, approximately ⅓ to ½ cup a day. He had no chest pain. No frequency, urgency, burning or pain on urination; no hematuria. No history of venereal disease. Family history was noncontributory.

Physical examination: The patient appeared to have lost weight recently. Head and neck were normal. Chest: slight kyphosis, anterior-posterior diameter increased; percussion note resonant throughout. Breath sounds normal throughout; no added sounds. There was a draining sinus from beneath the right scapula. Blood pressure 178/88, pulse 76, regular and moderately strong; left border of heart 4 inches from midline. No murmurs heard. Abdomen was symmetrical in

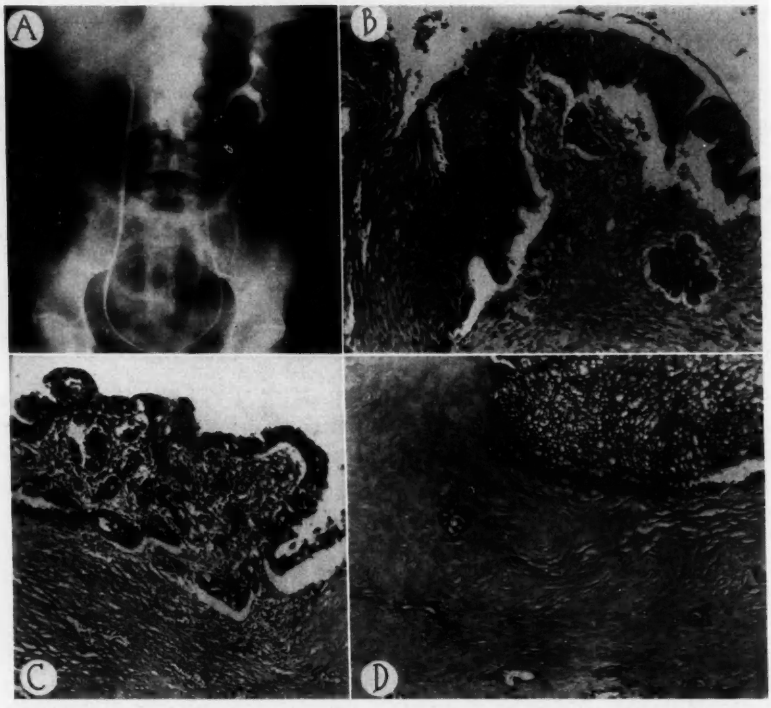

FIG. 9. Case 6. *A*, retrograde pyelogram showing obstruction at right ureteropelvic junction to the passage of dye. *B*, microscopic section showing invasive squamous cell carcinoma. Note stratified squamous epithelium on surface. *C*, microscopic section showing invasive squamous cell carcinoma at another site (mucicarmine stain). A few droplets of mucin are present in overlying epithelium. *D*, microscopic section showing intra- and extracellular mucin (mucicarmine stain).

shape and movement; no enlarged organs, masses or tenderness; hernial sites clear. On rectal examination, sphincter tone good; no abnormal tenderness; no masses palpable; prostate not enlarged; a few hemorrhoidal tags externally. The right testis was firmer and slightly larger than left; otherwise negative.

Laboratory findings: Urine: specific gravity 1.020, negative for albumin and sugar, on 2 occasions a trace of albumin, sediments revealed 5 to 10 white blood cells and a few granular casts. Blood: hemoglobin 86 per cent; white blood cells 9,000, packed cell volume 44; sedimentation rate 30. Stool: negative for occult blood. Biochemical: A.C. sugar 75. Serology: Kahn negative. Glucose tolerance curve: slightly prolonged hyperglycemia. Gastric analysis: essentially normal.

Cholecystogram revealed, March 14, a gallbladder of normal outline which concentrated dye moderately well; no evidence of stone formation. A chest film revealed old empyema in the right chest with surgical drainage. A zone of increased density in this region probably represented fibrosis following this disease. There was no definite evidence of active parenchymal disease at this time.

Barium enema: normal. The esophagus functioned very well in the supine and upright positions. There was no evidence of esophageal varices. Lumbosacral spine: There was definite evidence of hypertrophic spondylosis. There was disc degeneration between T-12 and L-1 and probably between L-1 and L-2. No disease in the sacroiliac joint.

Progress note: The patient was transferred to general surgery on March 30, 1955 for abdominal exploration. This was performed on March 31 at which time a small, hard, fixed mass was located in the right renal area. Subsequent report of the biopsy showed the presence of cells in nests of the signet ring variety. Postoperatively urological investigation was carried out. Retrograde pyelography showed the presence of a tumor of the right kidney; dye could not be introduced into the renal pelvis or calyces. The left pyelogram was normal. An aortogram was performed on April 16, 1955. The report in part was, "the right renal arteries are presumably obstructed since no dye has entered them."

On April 22, nephrectomy was performed. The kidney was found to be small, hard and fixed in position. By blunt dissection it was freed and removed. No bleeding was encountered from the pedicle; one small gelfoam pack was left in position.

The liver was seen to be greatly enlarged, but no nodules were palpable. Free fluid was present in the peritoneal cavity. Postoperative course uneventful to date.

Pathological report: Sections of perirenal tissue from the right side removed at laparotomy showed nests of epithelial cells in a connective tissue stroma. There were intercellular bridges in some of the nests and a few of the cells contained mucus.

The right kidney weighed 37 gm. It was firm in consistency and its thickened capsule was removed with difficulty from a pale grey, granular and pitted surface. The cut surface was grey in color and the interlobar and arcuate arteries presented as yellow streaks. Distinction between cortex and medulla was lost in multiple areas. The cortex measured up to 4 mm. in thickness. The calyces were slightly enlarged and irregular. They contained greyish gelatinous material. The epithelial surface of the calyces and the small pelvis was grey and granular. No plaques were present.

Four firm pieces of perirenal tissue, weighing 38 gm., were included with the kidney specimen. The cut surface of each piece was grey with irregular yellow-orange areas resembling adrenal cortex.

Multiple sections of kidney showed a marked fibrous replacement of cortex and medulla. The glomeruli for the most part were hyalinized and there was an infiltrate of lymphocytes in the interstitial tissue in those areas which were not replaced by dense scar. The large and medium sized arteries were almost completely obliterated by hyaline connective tissue. There was no amyloid in the kidney.

There was a carcinoma with multiple points of origin from the epithelial lining of the calyces. The tumor for the most part was squamous in type, with intercellular bridges and focal areas of keratinization. It infiltrated the small kidney diffusely and extended through the renal capsule into the perirenal tissues. Intracellular and extracellular mucus was present in many of the cell nests and

there were a few gland-like spaces filled with mucus. Pseudo gland formation due to cell degeneration was prominent.

The lining of the calyces between the areas of invasive carcinoma varied from a single layer of flattened epithelial cells to epithelium of the stratified squamous type with intercellular bridges. Only a few droplets of mucus were present in the epithelium where it was transitional in type. Diagnosis: Squamous cell carcinoma with glands and cells containing mucus (mucoepidermoid carcinoma of renal pelvis).

Case 7 (fig. 10). Papillary noninfiltrating carcinoma grade 2 of ureter; bronchogenic carcinoma.

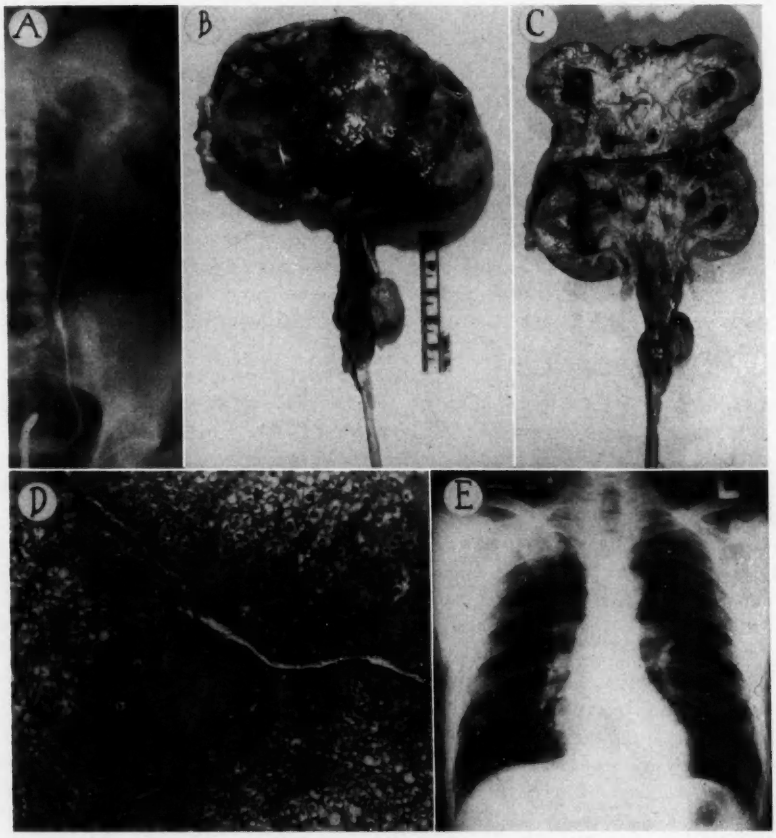

FIG. 10. Case 7. *A*, showing obstruction of dye near ureteropelvic junction on left side. *B*, gross specimen showing polypoid tumor in ureter. *C*, opened specimen showing hydronephrosis, and tumor in upper ureter. *D*, microscopic section showing thin branching connective tissue stalks covered by several layers of epithelial cells of a transitional type. Diagnosis: Papillary noninfiltrating carcinoma grade 2 of ureter. *E*, chest film showing lesion in right apex (bronchogenic carcinoma). (Reprinted by courtesy British Journal Urology; MacLean: Brit. J. Urol., **26:** 236, 1954).

S. B., aged 56, was admitted to Queen Mary Veterans Hospital on August 15, 1952 complaining of frequency and urgency.

The past history revealed that he had been under care of various D.V.A. hospitals since 1946. First admission was in October 1946 for chronic bronchitis and anxiety state. Second admission was in February 1947 for gross hematuria. He was found to have early middle lobe prostatic hypertrophy and prostatic calculi. No active treatment was instituted. The third admission was June 1, 1948 with the diagnosis of stricture of the urethra, mild hypertrophy of the prostate, and prostatic calculi. Dilatation of the urethra was carried out. There was no treatment given to the prostate. Excretory urography at this time showed no gross abnormality of either kidney. Kidney function appeared satisfactory. The fourth admission was in December 1949, as an outpatient, when he complained of his bronchitis, and "shakiness." The fifth admission to the Veterans Hospital was in March 1951, at which time a transurethral prostatic resection was carried out. The sixth admission was in July 1952 with the final diagnosis of phimosis, balanitis, left varicocele, chronic prostatitis, and chronic bronchitis. He was considered fit for work on discharge. One month later he was seen in the psychiatry section where a diagnosis was made of mental retardation and emotional instability.

Physical examination: Head and neck essentially normal. Thorax: Auscultation of the chest revealed sounds of fair quality in both lungs, with occasional rhonchi heard throughout both lung fields. The expansion was only fairly good on expiration. Heart normal. Blood pressure 155/100. Abdomen: There was a well healed appendectomy scar. Examination of the abdomen was otherwise normal; penis circumcised; testes normal; epididymides normal. Rectal: The prostate is slightly enlarged with increased fibrosis present. A previous diagnosis of prostatic calculi has been made.

Urine: Acid; specific gravity 1.025; albumin negative; sugar negative; microscopic: occasional pus cells seen and occasional epithelial cells.

Excretory urography showed nonfunction of the left kidney. At cystoscopy, the catheter was passed up the right ureter with ease to the renal pelvis. A catheter was passed up the left ureter as far as the transverse process of the third lumbar vertebra, where it met an obstruction. When dye was injected, the pyelogram on the right side was entirely normal. No dye passed beyond the point of obstruction at the third lumbar vertebra on the left side. The conclusion was that the patient had a nonfunctioning left kidney and that he probably had a nonopaque calculus on this side. It was decided therefore to explore the left kidney and ureteral region.

At operation on September 24, 1952, the point of obstruction in the ureter was felt and an incision made over it. Instead of a nonopaque calculus, a polypoid tumor of the ureter was found. A nephrectomy was done and included the upper 4 inches of ureter.

Pathological report: The pathological specimen showed a tumor mass in the ureter measuring 2 by 1.3 cm. It was attached to the wall of the ureter by a pedicle measuring 6 mm. in diameter, 2 cm. from the ureteropelvic junction. The pelvis was dilated.

Sections of tumor showed a poorly organized papillary growth. Several layers

of epithelial cells of the transitional cell type covered a thin framework of connective tissue. In many areas the papillary structure was lost and the tumor was composed of broad zones of epithelial cells separated by strands of vascular connective tissue. There was a corresponding variation in nuclear atypism in different areas. The wall of the ureter was not invaded. Diagnosis: Papillary noninfiltrating transitional cell carcinoma grade 2 of ureter; hydronephrosis and chronic pyelonephritis.

Progress: On the postoperative re-examination of the patient, some 2 months after discharge from the hospital, the chest x-ray revealed an area of infiltration in the right upper lung field. The patient was therefore readmitted to the hospital on February 11, 1953, when further investigation revealed that the infiltration in the right upper lung field was probably a bronchogenic carcinoma.

On April 23, 1953, a right upper lobe lobectomy was performed, with section of the glands at the hylar region. Microscopic sections of the tumor revealed it to be a bronchogenic carcinoma. Recovery was uneventful and he was discharged from the hospital on May 12, 1953.

Followup: Five months later, on September 14, 1953, the patient was admitted to another D.V.A. hospital where he died. At autopsy, the following findings were noted: Bronchogenic carcinoma of right lung (lobectomy right upper lobe); secondary carcinoma of regional lymph nodes, right adrenal gland; large bowel and abdominal lymph nodes; organizing pneumonia, bilateral; acute bronchopneumonia, bilateral; acute splenitis; chronic prostatitis; atherosclerosis of aorta and coronary arteries (moderate).

Case 8 (fig. 11). Papillary infiltrating transitional cell carcinoma grade 2 of ureter.

J. S., a man aged 70, was first admitted to the Royal Victoria Hospital in March 1948 at which time a two-stage suprapubic prostatectomy was done.

He was readmitted to the hospital on October 25, 1951 complaining of blood stained urine intermittently, of 10 months' duration. The urine would become grossly bloody for 1 to 2 days at a time, and approximately at 10-day intervals. Three months after the onset of the gross hematuria, the patient was investigated elsewhere and apparently told that there was decreased function of the left kidney. No specific recommendations were given to him at that time.

Physical examination: Head and neck entirely normal. Lungs normal. Heart not enlarged, no thrills, no murmurs, no irregularities. Blood pressure 120/68. Abdomen soft; well healed suprapubic scar. No costovertebral tenderness. No masses palpated. Liver and spleen not palpated. Neither kidney palpable. Genitalia normal. Rectal: sphincter tone normal; the prostatic bed was fibrous and firm.

Laboratory investigation: Urine: acid; specific gravity 1.008; albumin, a trace; sugar, negative; microscopic: scattered red blood cells; rare white blood cells.

Phenolsulfonphthalein test, 40 per cent in 2 hours.

Electrocardiogram normal; chest film normal.

Nonprotein nitrogen 23 mg. per cent.

Cystoscopy: Bladder was normal. Blood could be seen coming from the left ureteral orifice. A catheter was introduced. The catheter in the left ureter curled

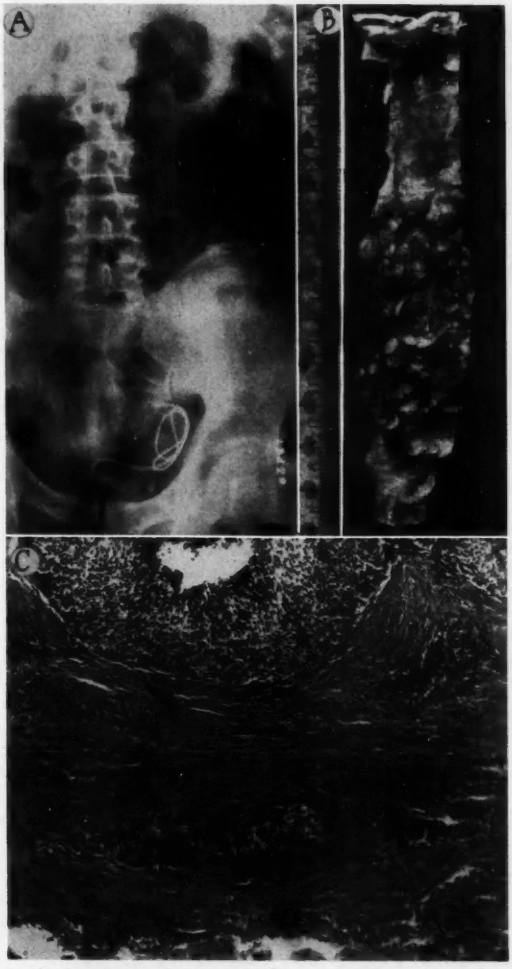

FIG. 11. Case 8. *A*, showing catheter coiled in left lower ureter. *B*, photograph of gross specimen showing carcinoma in ureter. *C*, microscopic section showing transitional cell carcinoma grade 2 of ureter, invading muscularis. Tumor was papillary on surface. (Reprinted by courtesy British Journal of Urology; MacLean: Brit. J. Urol., **26**: 235, 1954.)

up in the lower ureter; the one in the right side was passed to the renal pelvis. When dye was injected, a normal pyelogram resulted on the right side, but on the left side the dye just returned into the bladder.

Excretory urography showed a normal right kidney and ureter with a nonfunctioning kidney on the left side.

A diagnosis of tumor of the left lower ureter was made and on November 3, complete left nephroureterectomy was done.

Pathological report: The left kidney weighed 115 gm. The external surface was rough, being both nodular and granular. The pelvis and calyces were markedly dilated and the renal parenchyma was narrow. The proximal half of the ureter was dilated up to 1.6 cm. in diameter. Tumor was present in 6 cm. of the distal half of the ureter. It completely encircled and extended into the lumen as a papillary mass. Two small nodules were present in the mucosa distal to this.

Microscopic sections of the tumor showed a papillary transitional cell carcinoma which invaded smooth muscle of the ureter in multiple areas. There was moderate cellular pleomorphism and a moderate number of mitotic figures. The nodules in the adjacent mucosa had a similar histological appearance. Diagnosis: Papillary infiltrating transitional cell carcinoma grade 2 of ureter; hydroureter, hydronephrosis, and chronic pyelonephritis.

Followup: Recovery was uneventful, and the patient was discharged from the hospital on November 24, 1951. He was readmitted 4 months later on April 2, 1952 at which time he had a recurrence of tumor in the bladder. A suprapubic cystotomy with excision of the tumor and coagulation of the base were done. He had four subsequent admissions from June 1952 to January 1954. On two occasions recurrence of tumor in the bladder was found, and treated by fulguration endoscopically.

On the last admission on June 23, 1954, a cystoscopic examination revealed no evidence of recurrence of the tumor in the bladder.

Case 9 (fig. 12). Papillary infiltrating transitional cell carcinoma grade 2 of ureter.

C. W., a woman aged 71, was admitted to the Royal Victoria Hospital on January 13, 1951, complaining of gross hematuria of 2 week's duration. During this time she passed a great many clots as well, and the hematuria had not decreased. Some dysuria was present during the first few days but had practically disappeared. She had mild frequency attributed to drinking large amounts of water in an attempt to clear up the bleeding. She gave no history of passing any sand or gravel, and no history of chills or fever. There was no loss of weight or strength.

Nine years previously, the patient had gross hematuria which caused her admission to another hospital. At this time a pelvic repair was carried out. Detailed investigation of the urinary tract was not done.

Physical examination: Breasts normal. Normal percussion note throughout both lungs; diminished breath sounds at both bases; no rales. Heart slightly enlarged. First sound was very loud, the second was practically inaudible. No thrills, no murmurs, no irregularities. Blood pressure 145/90. Abdomen soft. Striae gravidarum. No masses palpated. Liver and spleen not palpated. Neither kidney palpable. There was no costovertebral angle tenderness. Extremities normal.

Laboratory investigation: Urine: grossly bloody; albumin 2 plus; sugar negative; microscopic: loaded with red blood cells, occasional pus cells.

Blood nonprotein nitrogen 36.6 mg. per cent. Creatinine 1.27 mg. per cent. Kahn: negative.

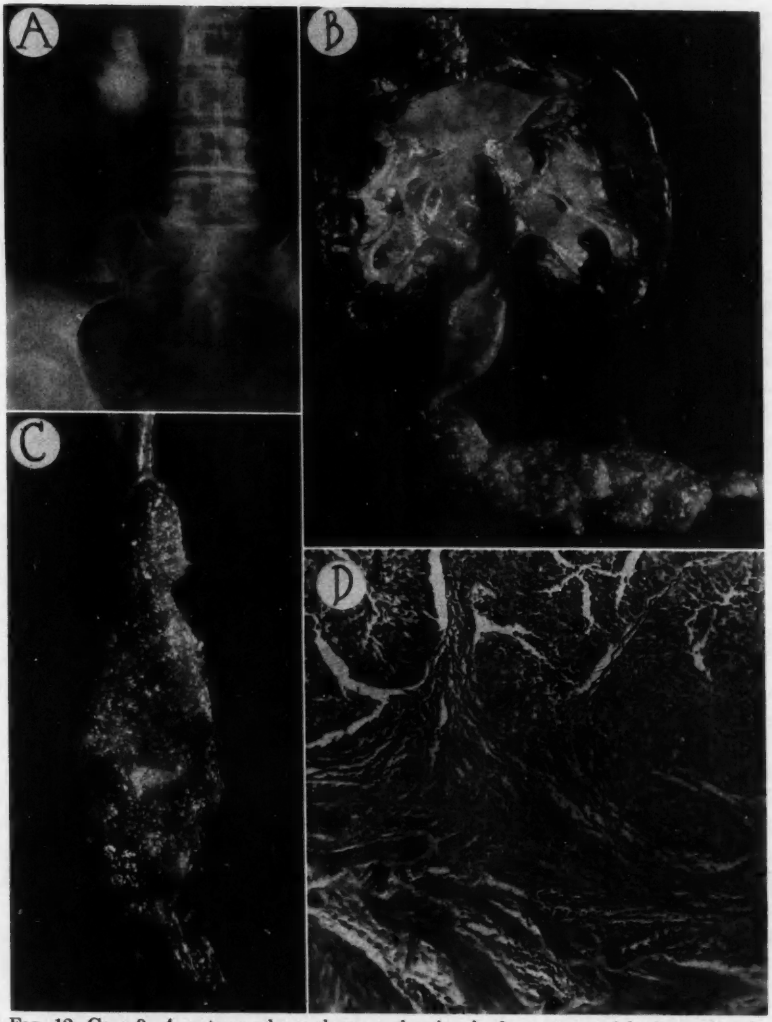

FIG. 12. Case 9. *A*, retrograde pyelogram showing hydroureter and hydronephrosis on right side. *B*, gross specimen showing kidney, and tumor in ureter. *C*, gross specimen showing closeup of tumor in ureter. *D*, microscopic section showing papillary transitional cell carcinoma grade 2, ureter. Note lymphocytic infiltrate at base.

Excretory urography revealed a normal sized kidney in normal position on each side. There were no opacities seen within the urinary tract. There was a calcified density in the region of the right bony pelvis which was probably the right ovary or a calcified fibroid. The left pyelogram was essentially normal. There was marked hydronephrosis and hydroureter on the right side.

Cystoscopy: The bladder was found to be inflamed and slightly ulcerated. The catheter was passed up the right ureter for 6 cm. at which point it met an obstruction. When dye was injected the ureter was seen to be very irregular.

A tentative diagnosis of tumor of the right ureter was made. A nephroureterectomy was advised, but refused.

The patient was discharged from the hospital and readmitted 1 month later (February 15, 1951) at which time a right nephroureterectomy was done. Recovery was uneventful.

Pathological report: The right kidney and attached 15 cm. of ureter weighed 135 gm. Only a few irregular, depressed areas were noted on the external surface. The cortex measured 4 mm. in thickness. The pelvis, calyces, and ureter were moderately dilated. The epithelial surface of the ureter commencing 6 cm. from the ureteropelvic junction and extending to within 1 cm. of the distal line of resection showed elevated granular and nodular greyish, mottled red and brown areas which completely encircled the lumen. The wall of the ureter in this area was thickened and its pliability impaired. Its outer surface was smooth and glistening.

Sections of ureter through various portions of the tumor as well as uninvolved areas showed the usual transitional epithelium changing abruptly to tumor tissue. The tumor was papillary in nature and infiltrated the muscularis of the ureter in a few areas. The cells were of the transitional type and varied somewhat in size and shape. A moderate number of mitotic figures were present. There was a heavy infiltrate of lymphocytes in the wall of the ureter.

The kidney was not remarkable except for some hydronephrosis. Diagnosis: Papillary infiltrating transitional cell carcinoma grade 2; hydroureter and hydronephrosis.

Followup: The patient was discharged from the hospital on March 14, 1951 and readmitted 1 year later on March 5, 1952 at which time she had a recurrence of the tumor in the bladder involving the whole trigone and the anterior wall of the bladder, just above the vesical neck. A suprapubic cystotomy was done and the areas were resected with the loop electrode and the bases thoroughly coagulated. The patient was discharged on April 10, 1952. Microscopically, the tissue showed papillary infiltrating transitional cell carcinoma grade 2.

She was readmitted 2 months later, June 3, 1952, at which time three small papillary growths were found in the bladder. These were all coagulated cystoscopically.

Case 10 (*fig. 13*). *Papillary infiltrating transitional cell carcinoma grade 3 of ureter.*

J. C. G., a man aged 73, was admitted to Ste. Anne's Military Hospital on December 11, 1946 in an emaciated condition, complaining of a poor appetite of 6 months' duration, and a crampy left lower abdominal pain with nausea and vomiting of 1 months' duration.

Physical examination revealed a very thin emaciated man. The head and neck were normal. The heart and lungs were normal. Blood pressure 130/75.

The liver was markedly enlarged; the right lobe felt very firm and irregular;

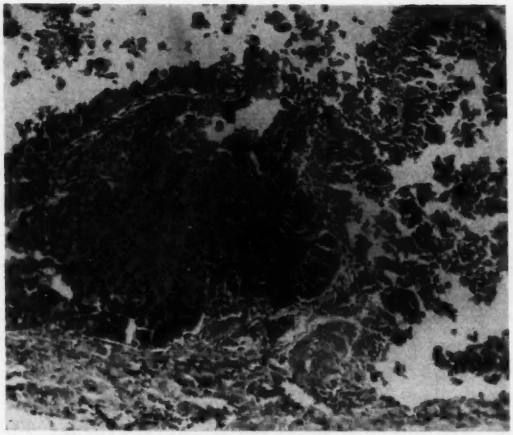

FIG. 13. Case 10. Microscopic section showing papillary transitional cell carcinoma grade 3, ureter. Note very large nuclei at base of tumor. Tumor extended through wall into periureteral fat in one area.

the left lobe could not be palpated. There was tenderness in the left lower quadrant of the abdomen, but no abnormal masses were palpated. Neither kidney was palpated. Genitalia were normal. Rectal: sphincter tone normal. Prostate: enlarged 1½ times normal size, fibroelastic, not fixed, not tender.

The patient died 3 days after admission to the hospital. An autopsy was performed. The essential findings are related below.

Autopsy findings: The right kidney weighed 89 gm.; 4 cm. of the ureter in its distal third was filled with a soft, friable tumor which encircled and invaded the wall. Small tumor nodules were present on the mucosal surface above and below the main growth. The ureter proximal to the lesion, and the pelvis were dilated.

Sections of the ureter showed a papillary tumor which extended through the wall into the periureteral fat. Cellular pleomorphism was marked.

The liver weighed 2980 gm. and the right lobe was almost completely replaced by metastatic carcinoma. There was also metastatic carcinoma in the para-aortic and iliac nodes. Diagnosis: Papillary infiltrating transitional cell carcinoma grade 3 of ureter; metastatic carcinoma in liver and lymph nodes (para-aortic and iliac); hydroureter and hydronephrosis; left kidney normal.

SECONDARY METASTASES TO URETER

In 1931 MacKenzie and Ratner reported 3 cases of secondary metastatic growths of the ureter. One was from an adenocarcinoma of the prostate and in 2 the primary growth was an adenocarcinoma of the stomach.

In the years 1932 to 1954 inclusive, there have been 10,223 successive autopsies at the Royal Victoria Hospital. In these 10,223 cases, secondary metastases of tumor to the ureter were found in 39 cases. Of these 39 cases, 18 had an actual lesion in the ureter, and 21 had a lesion surrounding the ureter and occluding it.

These 21 cases should not be considered as true metastatic lesions of the ureter. Of the 18 cases in which there was an actual lesion in the ureter, the primary lesion was in the bladder in 6; in 3 the primary tumor was in the kidney, and in 2 the primary lesion was in the renal pelvis.

This leaves only 7 cases in which the primary lesion was outside the urinary tract. The other sites involved were adenocarcinoma of the prostate 1, carcinoma of the rectum 2, carcinoma of head and body of pancreas 1, carcinoma of breast 1, carcinoma of the thyroid 1, and a melanoma metastasizing to the kidney and ureter 1. These 7 cases give an incidence of true metastases in the ureter from a primary tumor arising elsewhere in the body, but outside the urinary tract, of 0.07 per cent.

In the 21 cases in which the ureter was occluded by tumor surrounding it, the primary lesion was in the breast 2, ovary 2, cervix 10, rectum and sigmoid 4, lymphosarcoma of the jejunum 1, carcinoma of the prepuce 1, retroperitoneal lymphosarcoma 1. External occlusion of the ureter caused by metastases from a primary carcinoma elsewhere occurred in 0.20 per cent of the autopsies.

ENDOMETRIOSIS OF THE URETER

Endometriosis of the ureter is included for completeness and because of the fact that it might be mistaken as a primary neoplasm of the ureter, as pointed out by Randall in 1941, when reporting the first case.

O'Conor and Greenhill, in their excellent article on endometriosis of the bladder and ureter, reported a case of endometrioma of the urinary bladder, and another case of endometriosis of the ureter. They also discussed the three main theories advanced as to etiology.

There have been no known cases of endometriosis of the ureter at the Royal Victoria Hospital during the past 37 years.

METHOD OF SPREAD OF TUMOR AND SITE OF METASTASES

Metastases from tumor of the ureter occur relatively early. There may be a considerable degree of extension within the lumen of the ureter. Extension through the thickness of the ureter occurs relatively early due to the thin walled nature of the ureter.

When the lymphatics and the bloodstream are invaded, metastases may occur anywhere in the body. The common sites encountered are the local lymph nodes, liver, vertebra, lung, kidney, spleen, pancreas and brain.

METASTASES OF TUMOR TO THE RENAL PELVIS

Although secondary tumor metastases to the kidney are relatively common, metastases to the renal pelvis are quite rare.

The authors wish to report a case in which a hepatoma in the liver metastasized to the left renal pelvis. A staghorn calculus also was present in the renal pelvis. (This case is being reported separately by Lingard, MacLean, and Heustis.)

Case 11 (fig. 14). Metastatic carcinoma in the renal pelvis from primary carcinoma in the liver.

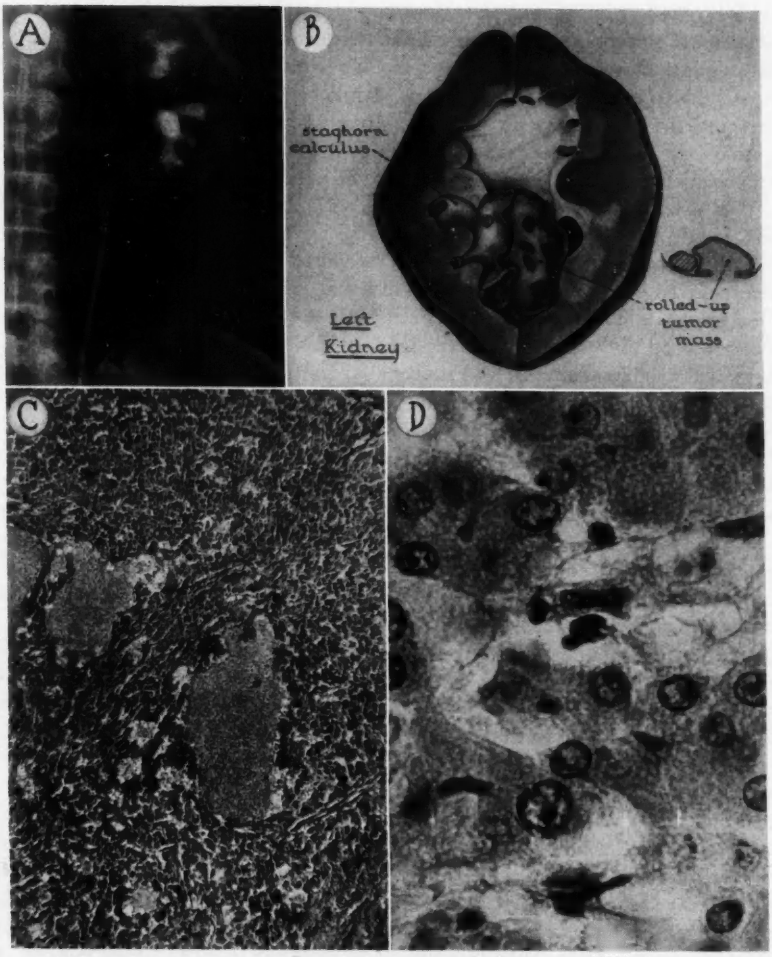

FIG. 14. Case 11. *A*, retrograde pyelogram showing filling defect in left renal pelvis and partial staghorn calculus. *B*, sectional drawing of kidney showing calculus and tumor mass in lower portion of renal pelvis. *C*, microscopic section of tumor showing cords of liver-like cells, blood sinuses and lakes. *D*, microscopic section of tumor from renal pelvis showing bile plugs.

A 60-year-old Chinese man was admitted to the urology service of the Royal Victoria Hospital in May 1954 with the complaints of gross hematuria, dysuria, and weight loss of 18 pounds over the past 10 months. The past history and family history were noncontributory. Gross hematuria had been present 10 months ago, 4 months ago, and for the 2 weeks immediately prior to admission. The blood was mixed throughout the urine. During the past 8 months, the nocturia amounted to three to four times per night. Physical examination re-

vealed some left loin tenderness. Neither kidney was palpable. The liver was not enlarged. The prostate gland was about twice normal size, fibroelastic, not fixed, not tender. There were no other palpable abdominal masses. The urine was grossly bloody and contained clumps of pus cells. The hemoglobin was 95 per cent and the nonprotein nitrogen was 19 mg. per cent. Cystoscopy revealed a normal lower urinary tract. Retrograde pyelography showed the presence of a large staghorn calculus occupying the lower half of the left kidney and dilated calyces. The right pyelogram was normal. Nephrectomy on the left side was performed May 15, 1954.

Pathological report: The left kidney measured 11 by 5 by 3 cm. The capsule was removed easily to show a smooth external surface. On section there was loss of corticomedullary demarcation in multiple areas and some of the pyramids were hemorrhagic. The calyces were moderately dilated and the internal surface of the pelvis was blood stained and roughened. In the lower part of the pelvis was a dark reddish mass of tissue resembling blood clot measuring 5 by 2 by 2 cm. This was loosely adherent to the internal surface of the pelvis. Cut surface of this mass was grey with irregular hemorrhagic areas. A staghorn calculus had been removed from the pelvis following nephrectomy. It was composed of apatite 60 per cent and struvite 40 per cent.

Sections of the kidney showed chronic pyelonephritis and in addition an acute inflammatory reaction with hemorrhage and necrosis in some of the pyramids and peripelvic tissues. The epithelium of the pelvis was eroded in some areas. Sections of soft tissue mass found within the pelvis showed it to be composed of columns of polyhedral epithelial cells separated by sinusoidal spaces filled with blood. Golden brown, bile-like plugs could be seen between the epithelial cells where they were arranged in solid groups. The structure and cellular appearance definitely resembled liver tissue.

Some sections through the renal pelvis in roughened areas showed the epithelium to be replaced by bile forming tumor cells. There was no invasion of muscle or blood vessels. Large blood lakes and areas of hemorrhage and necrosis were present in the tumor. Only a few of the epithelial cells had abnormally large nuclei; no mitoses were present. Some of the brown pigment gave a positive reaction with a histochemical test for bile and some of it gave a positive reaction for iron. Diagnosis: Metastatic carcinoma in the renal pelvis from a primary carcinoma in the liver. Followup: Two and one half months later, the patient was readmitted to the medical service complaining of anorexia of 3 weeks' duration and pain in the right upper quadrant of the abdomen. In addition he had become jaundiced and was passing light colored stools.

Physical examination revealed a cachetic man with markedly icteric sclerae. Coarse rales were heard throughout the right lung and abdominal examination revealed a palpable liver 10 cm. below the right costal margin. The hemoglobin was 42 per cent and the white blood count 22,000. About four hours following admission the patient's condition deteriorated rapidly and he expired.

Postmortem examination revealed the presence of primary carcinoma of the liver with multiple tumor nodules measuring up to 20 mm. in diameter present in the lungs and adrenals. The liver measured 22 by 26 by 10 cm. and was

greenish in color and friable in consistency. It weighed 2475 gm. A liver fluke infestation was found. Cholelithiasis and arteriosclerosis of the coronary arteries were concomitant findings. There was no tumor in the right kidney or in the lymph nodes.

SUMMARY AND CONCLUSIONS

Early in embryonic life, the bladder, ureter, and renal pelvis are lined with identical and continuous epithelium which is transitional in type. This explains why tumors arising in any of these areas are similar in type, and may be identical in histological appearance.

The effect of chronic irritation on the epithelium of the renal pelvis and ureter with resulting proliferative changes is discussed. Metaplasia to squamous epithelium or to mucin-secreting gland formation is discussed. A case showing mucinous metaplasia of the renal pelvis with mucin-secreting glands in the tunica propria is presented. This is a very rare type of case. Other cases showing proliferative irritative changes and squamous metaplasia are shown.

The significance of "predisposing factors" and of "seeding," in relationship to urinary tract tumors is discussed. The relationship of normally occurring steroids and of chemical carcinogens to the production of tumor in the urinary tract is noted.

There is a very high incidence of calculus present in tumors of the renal pelvis and ureter.

At the Royal Victoria Hospital, in the 30-year period from 1925 to 1954 inclusive, there were 4 cases of primary carcinoma of the ureter operated upon. In a 22-year period from 1932 to 1954, there has been 1 case of primary carcinoma of the ureter found in 10,223 successive autopsies. In the 8-year period from 1946 to 1954, in the Department of Veterans Affairs Hospitals in Canada, there have been 6 cases of carcinoma of the ureter operated upon, and 1 found at autopsy.

In the 15 years, 1917 to 1931, at the Royal Victoria Hospital (as reported by MacKenzie and Ratner) there were 96 cases of renal tumor operated upon, only 1 of which was a case of tumor of the renal pelvis. In the following 23 years from 1932 to 1954, there were 111 kidney tumors operated upon, of which 14 had primary carcinoma of the renal pelvis. In the 8-year period, 1946 to 1954, the Department of Veterans Affairs Hospitals in Canada had 164 cases of tumor of the kidney operated upon or found at autopsy, of which 18 were carcinomas of the renal pelvis. In the total series of 471 cases of kidney tumor, 33 were carcinomas of the renal pelvis, giving an incidence of 7 per cent.

Typical cases of tumor of the renal pelvis and ureter are presented, along with the microscopic sections. In addition, a case of squamous cell carcinoma of the renal pelvis and a case of an infiltrating squamous cell carcinoma of the renal pelvis containing mucin-secreting glands and cells are shown.

A case of metastases of a primary carcinoma of the liver to the left renal pelvis is presented. It was associated with a staghorn calculus.

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TREATMENT OF TUMORS OF THE RENAL PELVIS AND URETER

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All tumors of the renal pelvis and ureter need not and should not be treated the same. There are widely divergent views, however, concerning when and how different therapeutic plans can be utilized most advantageously. Any attempt to reiterate all of the opinions regarding treatment that have been expressed to date, or to evaluate critically the factual and theoretical evidence on which many contentions and convictions have been based, would be much more controversial than illuminative.

This presentation will consist of an analysis of 220 cases of primary neoplasm of the renal pelvis or ureter treated at the Mayo Clinic from 1910 through 1954. The series is presented not with any illusions that it represents ideal treatment of such tumors, but in the hope that the consolidated experiences of the 19 surgeons who operated on these patients may help to crystallize current therapeutic concepts.

Several factors had to be considered when the treatment of these tumors was planned. Sixty-eight per cent of the patients were in the sixth and seventh decades of life (table 1). Twelve per cent were at least 70 years of age. Males predominated in a ratio of 3:1.

Thirty-five per cent of the entire group also had serious unrelated diseases of other systems (table 2). Cardiovascular disturbances were the most common, but there was a surprising incidence of metabolic disorders. Eleven patients also had a second primary carcinoma.

In 32 per cent of the cases the lesions at the time of admission were not confined to the renal pelvis or to the ureter (table 3). Even those individuals who presented tumors of the pelvis or ureter alone frequently had multicentric growths. Twenty-five per cent of all patients with tumors in the renal pelvis also had similar lesions in the ureter. Twenty per cent of the entire group also had vesical tumors at the time of the initial examination at the clinic.

Forty-five per cent of the patients had either primary or secondary ureteral neoplasms. The location of these 98 tumors in the ureter is shown in table 4. Secondary lesions were a little more common in the upper third of the ureter when the primary growth was in the pelvis but almost as many patients with pelvic tumors had ureteral involvement confined to the lower third. Every conceivable combination of locations was encountered at least once. The lower third of the ureter contained tumor in 64 per cent of these 98 cases.

It is apparent, therefore, that irrespective of initial clinical impressions treatment of a substantial number of individuals had to be geared to elderly patients with serious concomitant diseases and a multicentric neoplastic process that involved both ends of the upper part of the urinary tract.

TABLE 1. *Age and sex distribution of 220 patients with primary tumors of the renal pelvis or ureter*

Age, Years	Sex		Total
	Males	Females	
25		1	1
30–39	7	1	8
40–49	29	6	35
50–59	54	15	69
60–69	57	23	80
70–79	19	7	26
83	1		1
Total	167	53	220

TABLE 2. *Serious unrelated diseases in 78 patients*

	Cases			Cases	
Cardiovascular		44	Other primary carcinomas		11
Hypertension	23		Colon	6	
Coronary occlusion	7		Ovary	2	
Arteriosclerotic heart disease	6		Prostate	2	
Rheumatic heart disease	3		Breast	1	
Parkinsonism	3		Others		10
Auricular flutter	2		Duodenal ulcer	4	
Metabolic		13	Syphilis of central nervous system	3	
Diabetes mellitus	10		Severe psychosis	2	
Exophthalmic goiter	3		Cirrhosis	1	

TABLE 3. *Location of tumors before operation in 220 patients*

Primary in	Alone	With Involvement of			Total
		Ureter	Bladder	Both	
Pelvis	109	27	13	13	162
Ureter	41		17		58

TABLE 4. *Location of ureteral tumors in 98 patients*

Segment of Ureter	Primary in		Total
	Ureter	Pelvis	
Upper	9	16	25
Middle	7	2	9
Lower	36	11	47
Upper and middle	1		1
Upper and lower	1		1
Middle and lower	1	2	3
All	3	9	12

TYPES OF OPERATIONS

The various surgical procedures that were employed conformed to the categories shown in table 5. Although nephroureterectomy was performed in two stages as early as 1917, radical operations failed to attain much favor until the late 1930's. It must be noted, however, that relatively few patients with tumors of the renal pelvis and ureter received any surgical treatment during the first 15 years covered by this study.

Nephrectomy and partial ureterectomy. Eighty-six patients had nephrectomy and only partial ureterectomy for the following reasons: regional metastatic lesions already obvious at operation, 40 cases; nonpapillary neoplasm without gross metastasis, 16; precarious condition of patient at time of operation, 16; patient died before contemplated second stage could be performed, 2; refused another operation, 1; treated during very early years covered by study, 11.

It must be conceded that in at least 56 of these cases removal of the remainder of the ureter would have had no real therapeutic value. Most of the dissections of regional lymph nodes in this series were in patients who already had lymphatic metastasis.

Subtotal nephroureterectomy. This term is used for operations that did not include removal of the intramural segment of the ureter. In some instances this segment was fulgurated from above, but in most of the cases the ureter was merely ligated and divided flush with the bladder. The interval between operations for the five patients who were treated in two stages varied from 7 to 19 months with an average of 11 months.

Complete nephroureterectomy. This group included excision of the ureteral orifice and variable amounts of the contiguous vesical wall. In 18 two-stage procedures the interval between operations varied from 10 days to 29 months. Only seven patients had the remainder of their ureter removed within 2 months. The average for the others was 13 months.

TABLE 5. *Surgical procedures employed in 220 cases*

Procedure	Date of Operation					Total
	1910–14	1915–24	1925–34	1935–44	1945–54	
Nephrectomy and partial ureterectomy	2	10	19	30	25	86
Subtotal nephroureterectomy						
1 stage		1	4	7	6	18
2 stages				3	2	5
Complete nephroureterectomy						
1 stage			7	27	40	74
2 stages		4	4	5	5	18
Excision of stump (nephrectomy elsewhere)			1		4	5
Partial ureterectomy			1		3	4
Removal of tumor only			1		2	3
Exploration and biopsy				3	4	7

TABLE 6. *Postoperative complications*

Operation*	Died in Hospital	Major Nonfatal Complications				Total
		Pulmonary	Cardiac	Incisional	Others	
Nephrectomy and partial ureterectomy (86)	6	7		4	1	18 (21%)
Subtotal nephroureterectomy (23)	1	4		2	1	8 (35%)
Complete nephroureterectomy (92)	1	4	2	4	2	13 (14%)
Excision of stump (5)		1				1
Partial ureterectomy (4)			1			1
Removal of tumor only (3)						
Biopsy only (7)		1				1

* Numbers in parentheses represent total patients who underwent designated operations.

Excision of ureteral stump. Five patients had nephrectomy elsewhere but came to the clinic with tumors in the remaining ureteral stumps. In one case, 10 years had elapsed since removal of the kidney. The average interval since initial operation for the others was 17 months.

Regardless of the reason that prompted deferment of the ureterectomy in the three groups just described, unless both stages of nephroureterectomy were completed during the same hospital admission there was an overwhelming tendency for patients to procrastinate about returning. Apprehension and a false sense of security due to lack of symptoms were potent motivating factors in many cases.

Partial ureterectomy. Four patients had only the tumor-bearing lower portion of the ureter excised. One of these died before the kidney and remainder of the ureter could be removed. The other three patients had diminished renal reserve and in each case the ureter was reimplanted in the bladder.

Removal of tumor only. One patient had a papillary tumor in the pelvis of his only kidney. This was treated by electroresection and coagulation, and the case was reported in detail by Ferris and Daut.[1] Another individual had a papillary tumor of the ureter without gross invasion and it was removed in the same manner. The third patient had a pedunculated growth arising from the intramural portion of the ureter and this was excised suprapubically after meatotomy.

Exploration and biopsy only. In seven cases it was apparent at operation that the patient was incurable, so only enough tissue was removed to confirm the diagnosis.

COMPLICATIONS

Deaths. Eight patients died 6 to 26 days after operation. Although several patients had more than one operation, only 3.6 per cent of these 220 patients failed to survive their surgical procedures.

[1] Ferris, D. O. and Daut, R. V.: Epithelioma of the pelvis of a solitary kidney treated by electrocoagulation. J. Urol., **59**: 577–579, 1948.

Six of the eight fatalities followed simple nephrectomy and partial ureterectomy. Admittedly, this group contained the worst tumors and the poorest surgical risks. Three patients died of pneumonia and two died of pyelonephritis, all five of whom were treated before the advent of sulfonamides. The sixth death in this therapeutic group was due to hemorrhage when an extensive carcinoma of the ureter eroded the iliac artery.

There was one death from myocardial infarction (proved by necropsy) 6 days after a one-stage subtotal nephroureterectomy. Another patient died of proved pulmonary embolism 10 days after the second stage of complete nephroureterectomy.

Early nonfatal complications. The distribution of 34 major but nonfatal postoperative complications is shown in table 6. Pulmonary disturbances were the most common and consisted of pneumonia, atelectasis and infarction.

There was one case each of cardiac decompensation and severe paroxysmal tachycardia. Another patient had cardiac arrest during nephroureterectomy, but this was detected immediately and prompt thoracotomy with cardiac massage permitted completion of the operation and prevented cerebral damage.

In four patients abscesses developed in the incisions. Two others had sufficient separation of the wound to require secondary closure, and four more had incisional hernias. Two of the hernias were in the lumbar region and the other two occurred in oblique incisions in the lower part of the abdomen through which the lower portion of the ureter had been removed.

Other complications included one case each of transient brachial palsy, excessive bleeding (controlled by ligation of the vessel in the retroperitoneal fossa), and vesicovaginal fistula. The fistula followed fulguration of the intramural portion of the ureter during subtotal nephroureterectomy and required surgical closure.

Complete nephroureterectomy seemingly does not entail any more hazards than does less radical procedures, but it is possible that some of the 23 patients who were treated in two stages might have had difficulty after a more prolonged single operation.

Subsequent tumors. Recurrent or new neoplasms were the most disturbing late complications. Table 7 includes all patients who survived operation and had any type of followup. Some have been traced for less than 5 years, but most additional tumors tend to manifest themselves soon after the initial operation. Not

TABLE 7. *Subsequent similar tumors*

Operation	Patients Followed	Site		Per Cent
		Ureter	Bladder	
Subtotal nephroureterectomy	22	2	12	64
Complete nephroureterectomy	89		38	43
Excision of stump	5			
Partial ureterectomy	3		2	
Removal of tumor only	3	2		

all of the patients that have been included returned to the clinic for re-examinations, and information for those who did not return had to be obtained from other sources. The statistics presented in table 7, therefore, must be accepted as conservative or minimal for subsequent tumors.

Recurrent tumors, new growths or residual carcinomas were noted in the incisions, ureteral stumps and bladders of some patients treated solely by nephrectomy and partial ureterectomy, but they were relatively uncommon. This entire therapeutic group has been omitted from this part of the study because papillary neoplasms were rare and few patients lived long enough for adequate appraisal. Those patients who were merely subjected to exploration likewise contribute little to this phase of the review.

At least 43 per cent of the patients who had complete nephroureterectomy required treatment of subsequent tumors of the bladder (table 7). An even higher percentage of those treated by subtotal nephroureterectomy had similar experiences. New growths in the intramural segment are more common than table 7 implies, for several patients who had subtotal nephroureterectomy elsewhere have appeared at the clinic with more carcinoma in this location.

Two of the patients who had only the tumor-bearing segment of ureter removed have had subsequent tumors in the bladder. In two of the three patients who had only their tumors removed, recurrent tumors eventually developed at the same sites.

It is obvious, therefore, that even radical procedures do not justify subsequent clinical negligence or apathy.

LATE RESULTS

There is only one true index of the efficacy of any operation, namely, long-term survival. Table 8 shows the number of patients who lived 5 or more years after operations performed prior to 1950. Ninety-four per cent of the patients treated from 1910 through 1949 were traced.

As might be expected, both types of nephroureterectomy produced better results than did simple nephrectomy. Although the group that underwent the subtotal procedure is not comparable numerically with the group that underwent the complete operation, the respective survival rates are almost identical despite any previously noted difference in the incidence of subsequent tumors. Even though the time interval tended to be unduly long between operations in the two-stage procedures, there was no significant difference in the 5-year survival rates for one-stage and two-stage operations.

Although 60 of the traced 157 patients survived for at least 5 years, not all were "cured." Only 33 (21 per cent) were alive at the time of last report. Three of these living patients had nephrectomy and partial ureterectomy, five had had subtotal nephroureterectomy, 24 had had complete nephroureterectomy and one patient had had only the tumor removed. The elapsed time since operation for these 33 individuals ranged from 6 to 19 years, with an average of 9 years.

Twenty-seven patients lived for at least 5 years but died after an average survival of 10 years. Ten are known to have died of unrelated diseases. Ten

TABLE 8. *5-Year survival rates by type of operation for patients seen in the period 1910–1949*

	Patients		Lived 5 or More Years after Operation	
	Total	Traced	Number	Per cent*
Nephrectomy and partial ureterectomy	69	64	13	20.3
Subtotal nephroureterectomy	19	19	10	52.6
Complete nephroureterectomy	68	63	34	54.0
Excision of stump	2	2		—
Partial ureterectomy	1	1		—
Removal of tumor only	3	3	3	—
Biopsy only	5	5		—
Total	167	157	60	38.2

* Based on traced patients. Inquiry as of January 1, 1955.

others are known to have succumbed to metastasis as late as 17 years after operation. Causes of death in the other seven are unknown.

Patients who were treated conservatively did not fare as well as table 8 implies. The one with partial ureterectomy was dead in 3 months. Two who had only their tumor removed died 6 and 13 years later with recurrent lesions. One patient who had a fibromucous polyp protruding from the right ureteral orifice was living 9 years after suprapubic excision. This case was reported in detail by Palmer and Greene.[2] The patient, a woman, was re-examined at the clinic on June 2, 1955, and there was no recurrence of her polyp and no evidence of any new growths. It is noteworthy that this is the only case of benign polyp of the upper part of the urinary tract on record at the Mayo Clinic in more than 2,000,000 patients, at least 250,000 of whom had complete urologic investigation.

Many of the 220 patients included in this series probably were doomed regardless of the type of operation that might have been performed. Others perhaps might still be living if less radical procedures had been employed. The grade of malignancy alone was not an accurate index of success or failure. A few individuals who had grade 4 lesions are living and well while others who had grade 1 tumors have died of metastasis. The presence or absence of infiltration seemed to be of paramount significance. But the subject of prognosis has been assigned to another participant in this symposium and is not within the scope of the current discussion. All of the tumors in this series are being restudied histologically and the results will be included in a later paper.

TYPES OF INCISIONS

Eleven simple nephrectomies were performed transperitoneally through anterior incisions while the extraperitoneal lumbar approach was used in 75 cases. The twelfth rib was resected in 12 patients. Clamps were left on the renal pedicle for 2 to 5 days in 11 instances. The transperitoneal operation did not enhance the final result.

[2] Palmer, J. K. and Greene, L. F.: Benign fibromucous polyp of the ureter: Report of a case. Surgery, **22**: 562, 1947.

Exploration and biopsy were performed through an anterior rectus incision in four cases and via the flank in the three others. The transperitoneal approach seemed to have special merit only when lesions of adjacent organs had been suspected.

Partial ureterectomy, removal of ureteral tumor only and excision of the ureteral stump after nephrectomy elsewhere were accomplished through either midline suprapubic or oblique lower abdominal incisions. There appeared to be a slight preference for the midline exposure irrespective of the side that was involved.

Several types of exposure were used for nephroureterectomy. Four patients had only anterior rectus incisions. In two cases, only generous anterior extension of the conventional lumbar approach was employed. Two separate incisions were used in 102 cases. The usual flank incision was combined with a midline or rectus incision in 58 operations and with an oblique, lower-quadrant approach in 44 procedures. Occasionally, removal of the cuff of bladder proved to be rather difficult through oblique incisions. It is noteworthy that there were no hernias after midline exposure.

In seven cases a modified Cherney incision was used for complete nephroureterectomy or removal of the ureteral stump after nephrectomy elsewhere. This approach was mentioned in a previous publication[3] and has been found to have distinct advantage over any combination of incisions in properly selected cases. It has been invaluable when dealing with questionable lower ureteral lesions, especially in obese individuals, but should not be tried if the kidney occupies an unusually high position.

TECHNIQUE

The patient is left supine and a small sandbag is placed under the ipsilateral side of the chest to rotate the flank forward. A transverse incision is started near the midline 2 fingerbreadths above the symphysis pubis, curved upward medial to the anterior superior spine of the ilium and extended into the flank as far as may be necessary (fig. 1).

After incision of the anterior sheath of the rectus and the aponeuroses of the external and internal oblique muscles, the transverse fascia is divided and the peritoneum is freed by blunt dissection. The contiguous oblique and transverse muscles are cut as far into the anterior portion of the flank as may be necessary (fig. 1).

The entire ureter and lower pole of the kidney are exposed promptly by retracting the peritoneum medially (fig. 2). If exposure of the bladder is inadequate, it can be improved by severing the rectus tendon on that side. The upper pole of the kidney may have to be freed blindly but the renal pedicle can be visualized without difficulty by retracting Gerota's fascia and the perirenal fat. The distal portion of the twelfth rib can be resected if necessary. If intraperitoneal exposure is deemed advisable, it can be accomplished promptly and efficiently.

[3] Culp, O. S. and DeWeerd, J. H.: Advantages of the Cherney incision for urologic operations. J. Urol., **69:** 445–453, 1953.

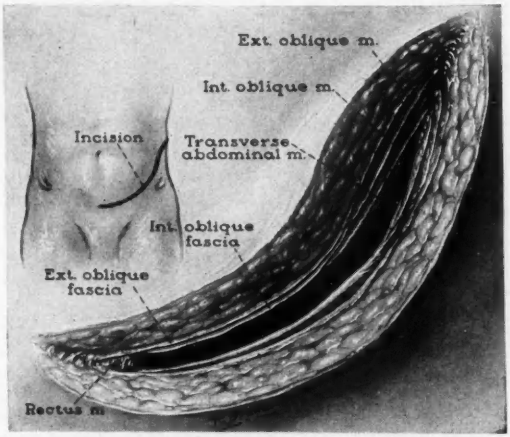

FIG. 1. Location of single incision for nephroureterectomy. Anterior sheath of rectus and aponeuroses of external and internal oblique muscles are incised. Muscles in flank are divided as far as necessary.

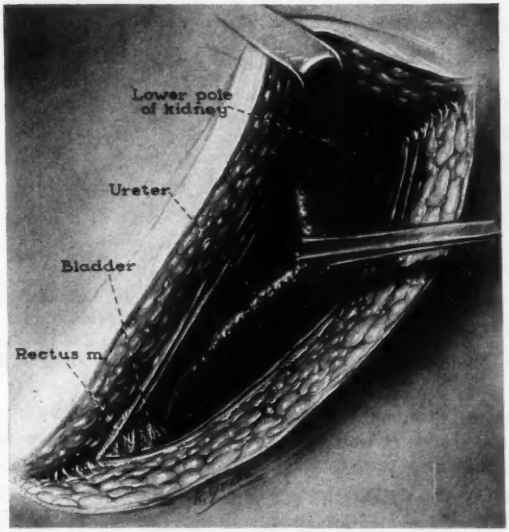

FIG. 2. Lower pole of kidney, entire ureter and adjacent portion of bladder exposed by retracting peritoneum medially.

The incision is closed with two layers of chromic catgut in the muscles and aponeuroses (fig. 3), plain catgut in the subcutaneous fat and nonabsorbable sutures in the skin. Drains can be brought out at either or both ends of the incision.

The length of incision necessary in a man who weighed 240 pounds is shown in

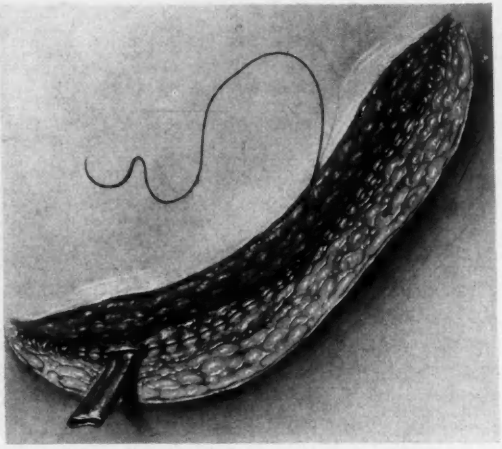

FIG. 3. Closure of incision with two layers of chromic catgut sutures in muscles and fascias after insertion of Penrose drain.

FIG. 4. Modified Cherney incision used for nephroureterectomy in a man who weighed 240 pounds. Note abdominal and lumbar scars of previous operations on same kidney.

figure 4. There had been two previous operations on this kidney. One had been performed transperitoneally and the other via the flank. Much shorter incisions will suffice in less obese patients. An abbreviated version of the same type of exposure was used for removal of the ureteral stump from a man who weighed 280 pounds (fig. 5). An earlier attempt elsewhere through a midline incision had been unsuccessful.

This type of incision does not appear to entail any increased postoperative morbidity, and meticulous closure of even the very long incisions requires less total operating time than do two independent incisions.

OTHER THERAPY

During the same period covered by this study, at least 4 patients (not included in the tables) had only endoscopic treatment. Each had a tumor at the ureteral

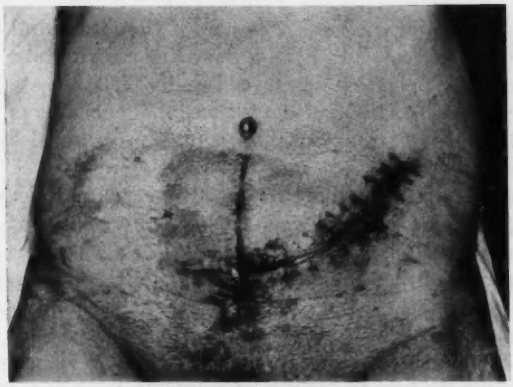

FIG. 5. Shorter modification of Cherney incision used for excision of ureteral stump in a man who weighed 280 pounds. Note midline scar of previous unsuccessful attempt.

orifice. More energetic therapy seemed to be contraindicated for several reasons. For example, a man, age 58 years, had active advanced bilateral pulmonary tuberculosis and a papillary tumor protruding from the right ureteral orifice. The orifice was dilated with a panendoscope, the tumor was avulsed and the base was fulgurated. He died of tuberculosis 3 years later.

Intramural tumors after subtotal nephroureterectomy usually were removed with the resectoscope.

Irradiation appeared to have only palliative value. There was no evidence in this study to refute Dean's statement that "I know of no benefit to be expected from prophylactic irradiation in these cases because it has never accomplished tumor destruction nor is there clear proof of tumor inhibition."[4]

Associated neoplasms of the bladder were treated by transurethral resection, suprapubic coagulation, segmental resection, use of radon seeds and total cystectomy. These adjuncts must be accepted as an essential part of the management of some patients with tumors of the renal pelvis and ureter. Choice of methods will vary just as it does in cases of primary vesical carcinoma.

CONCLUSIONS

After an analysis of 220 cases of primary tumor of the renal pelvis or ureter treated at the Mayo Clinic and a survey of most of the other reviews of the subject, it is apparent that several basic therapeutic tenets are here to stay.

Nonpapillary neoplasms are not likely to produce similar lesions at a lower level and little is to be gained by routinely removing all of the ureter on the affected side. Results in this group are so poor that more consideration must be given to dissections of regional lymph nodes even though it has yet to be proved that anyone with evidence of nodal involvement is still "curable."

Nephroureterectomy should be mandatory in all cases of papillary carcinoma of the upper part of the urinary tract unless there already is evidence of metas-

[4] Dean, A. L.: Tumors of the Kidney, Pelvis and Ureter. In Campbell, M. L.: Urology. Philadelphia, W. B. Saunders Co., 1954, vol. 3, p. 2153.

tasis. There will be fewer subsequent tumors if the intramural portion of the ureter is also excised. Removal of the kidney and entire ureter should be accomplished at a single operation whenever possible. If a two-stage procedure is dictated by the general condition of the patient, the remainder of the ureter had best be excised during the same hospital admission to avoid excessive delays between stages.

Unique situations, especially depleted renal reserve, may demand conservative operations, but these should be viewed as practical solutions to embarrassing predicaments rather than operations of choice.

Deliberate removal of the tumor alone in the presence of a normal upper tract on the opposite side is a therapeutic gamble and a philosophic challenge. Benign lesions undoubtedly occur but they are so rare that there is some question as to whether or not the measures necessary to identify most of them represent sound surgical judgment or the best operative technique. Any papillary tumor that does not invade the base can obviously be excised in toto, and not all such patients will necessarily experience additional similar or more malignant neoplasms. But as yet there is no way of knowing the tumor-forming potential of any patient. Even after radical treatment under the most encouraging circumstances, the results have left much to be desired. To leave a concealed segment of urothelium that already has produced one tumor is a much greater risk than is the possibility of neoplasm in the opposite ureter or renal pelvis. There were no examples of bilateral tumors in this series of 220 cases but they are known to occur. The judicious use of conservative operations in otherwise healthy patients will require a degree of uncanny foresight that has been denied most surgeons.

Too frequently, patients are found to be incurable. Heroic surgical measures under such circumstances offer only physical trauma for the patient and technical exercise for the surgeon.

PROGNOSIS OF PRIMARY TUMORS OF RENAL PELVIS AND URETER

JOHN E. DEES

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After reviewing the recent literature on primary tumors of the renal pelvis and ureter and their prognosis, I find that the subject does not lend itself well to statistical analysis. The clinical material is so varied, and tabulated in such different ways, that one is unable to tell exactly how many of each type of tumor have been reported, nor how many have had either nephrectomy or nephroureterectomy with or without excision of a segment of the bladder. The number of patients who have lived 1, 3, 5, or 10 years without recurrence cannot be accurately determined. In addition, it is impossible to determine from many of the recorded reports whether the individuals were potentially curable by surgery because of inadequate information about the presence or absence of metastases or local extension at the time of operation. There is also no uniformity in pathological descriptions, nor in the followup studies. These are not faults of the capable authors who have recorded their findings nor inadequacies in their methods of studying the patient. They are inherent variables in a complex problem. Rather than to attempt a tabulation of all the reported series for this symposium it has seemed to me that a more profitable approach is to select for discussion, a few of the carefully studied and followed groups of patients and to report our own experience.

To illustrate the difficulty in comparing the larger reported series of patients is the excellent report of Scott in 1943 on 149 patients with primary carcinoma of the ureter who were operated upon. Thirty-two patients were reported well when last seen, but of these only 6 were observed for more than 4 years. In 182 cases of primary tumor of the ureter which he collected, there were 22 different pathological diagnoses and considerably more than 12 different kinds of operation. The next similar report by Senger and others in 1953 analysed an additional 130 cases of their own and from the literature. Fifty-two of this collected group had shown no evidence of recurrence, but of these, 50 per cent had been followed for less than 1 year. This again emphasizes the difficulty in establishing prognosis even from such an impressive collection of cases.

A possible exception to the foregoing is the prognosis of squamous cell carcinoma of the renal pelvis or ureter. The results of treatment are so uniformly poor in this condition that no long period of followup is usually necessary to know what happens to the individual patient. In 1949 Gahagan collected 196 cases of squamous cell carcinoma of the renal pelvis from the literature and found no 5-year cure reported. Since then cases reported by Oberkircher, Riches, and the 4 cases to be reported herewith bring the total to at least 275. In none of these additional cases has a 5-year cure been reported. It would seem probable that this currently hopeless prognosis of squamous cell carcinoma of the upper urinary

tract is due to the fact that these tumors produce symptoms late in the course of the disease. Silent hematuria is by far the most common early symptom of all urothelial tumors while pain or symptoms of infection or obstruction appear later. Papillary tumors characteristically produce luxuriant growth within the lumen of the pelvis or ureter and the trauma from peristalsis produces gross hematuria quite early as a rule, often before significant spread has occurred. Bleeding from squamous cell carcinoma, on the other hand, is late and is usually due to necrosis secondary to invasion and obstruction of nutrient blood vessels. Furthermore, these tumors are apt to be of a high degree of malignancy from a histological and biological standpoint as opposed to the slight evidence of malignancy seen in some of the transitional cell tumors.

Riches has recently reported 147 operable cases of transitional cell carcinoma of the renal pelvis collected in Great Britain. Of 79 cases with no involvement of the ureter or bladder, 62 per cent survived for 1 year and 41 per cent for 10 years. Of the 68 cases where the ureter or bladder was involved, although 71 per cent survived for 1 year, only 33 per cent survived for 3 years. Accordingly, he felt that involvement of the ureter or bladder made the prognosis of a primary carcinoma of the pelvis much more grave. Of 61 cases of benign papilloma of the renal pelvis which were followed for more than 1 year after nephroureterectomy 95 per cent survived for 1 year, 87 per cent for 3 years, and 50 per cent for 10 years. Perhaps the best results obtained to date are those reported by O'Conor with 8 of 12 cases of papillary carcinoma of the pelvis surviving without evidence of recurrence for from 4 to more than 10 years after operation. In contrast, Foot reports that of 19 patients who had nephrectomy for transitional cell carcinoma of the pelvis, only 1 lived for 5 years after operation and he died of cancer in the seventh year.

A most interesting report on 33 cases of primary carcinoma of the ureter from the Mayo Clinic has recently been made by Whitlock and others. Of this group,

TABLE 1. *Results of treatment of primary tumors of renal pelvis and ureter*

	Years after Operation								
	0–1	1–2	5–6	6–7	7–8	14–15	17–18	Total	
Transitional cell ca. of pelvis									
Living			1	1*	1		1	4	10
Dead	5	1						6	
Squamous cell ca. of pelvis									
Living		1						1	2
Dead	1							1	
Benign papilloma of pelvis									
Living					1	1		2	2
Dead								0	
Transitional cell ca. of ureter									
Living	4							4	8
Dead	1	3						4	

* Recurrent tumor present.

17 were purely superficial without involvement of the submucosa although histologically of varying degrees of malignancy. Of those operated upon more than 3 years previously, 81 per cent survived; and of those operated upon more than 5 years previously, 66 per cent survived. Of the 16 remaining patients in this group whose tumor showed infiltration of the ureteral wall only one survived for more than 3 years and he had extensive carcinoma at the time of his last examination. Six of O'Conor's 8 cases of primary papillary tumor of the ureter survived from 2 to 11 years after operation, but the pathological findings in these cases are not described.

The results of treatment of 22 patients with primary tumors of the renal pelvis or ureter at Duke Hospital are depicted in table 1. Four cases of transitional cell carcinoma of the pelvis are living for almost 6, 7, 8, and 18 years respectively since operation, although the 7-year survivor had recurrent tumor present in her bladder when last examined. To re-emphasize the difficulty in prognosis it is interesting to note that at the time of operation, the 18-year survivor operated upon by my associate, Dr. E. P. Alyea, had a large mass of tumor extending down the lumen of the renal vein to its junction with the vena cava. There was another tumor thrombus in the spermatic vein, and invasion of the renal parenchyma from the renal pelvis to, but not through, the capsule. Five patients died within 1 year after operation and another within 2 years. Of 2 cases of squamous cell carcinoma of the pelvis, 1 is living less than 2 years postoperatively and 1 died within 1 year after operation. The 2 cases of benign papilloma of the pelvis are living for 8 and 15 years postoperatively, with no evidence of recurrence. Each had simple nephrectomy. Of 8 cases of transitional cell carcinoma of the ureter, 4 were last known to be living but for less than one year after operation. Two of these have been operated upon within the last year whereas the other 2 could not be followed. The remaining 4 are known to be dead in less than 2 years after operation.

The results in untreated patients with primary pelvic tumors are shown in table 2, the diagnosis being made either at autopsy or at palliative operation. Three patients with transitional cell carcinoma died within 1, 3, and 4 years respectively, and 2 patients with squamous cell carcinoma died within 1 and 2 years respectively, after the onset of symptoms.

TABLE 2. *Results in untreated primary tumors of renal pelvis**

	Years after Onset of Symptoms				
	0–1	2–3	3–4	Total	
Transitional cell ca. of pelvis					
Living				0	3
Dead	1	1	1	3	
Squamous cell ca of pelvis					
Living				0	2
Dead	1	1		2	

* Diagnosis at autopsy or palliative operation.

It is generally accepted that primary tumors of urothelium have similar histologic and biologic characteristics whether their primary point of origin is in the renal pelvis, ureter or the bladder. Histologically, whether composed of transitional or squamous cells their site of origin is indistinguishable unless the examiner is oriented by the presence of adjacent tissue from the various levels of the urinary tract. Their histologic picture may vary from a benign orderly growth to a wildly undifferentiated cellular pattern. Whether benign or malignant, transitional cell tumors are prone to implant upon and produce secondary tumors in sites of the urinary tract below their point of origin. If this were the only factor to be considered in prognosis, one would expect that a primary tumor of the renal pelvis would offer a much worse prognosis than one of the same histologic characteristics originating in the ureter, but this is not so. Among the many factors influencing the prognosis of tumors of the renal pelvis and ureter, the depth of invasion is probably of even greater significance than it is in affecting the prognosis of primary bladder tumors. In the ureter, or in the extrarenal portion of the pelvis the neoplasm must penetrate to a depth of only a mm. or slightly more to invade the rich periureteral lymphatics. The renal parenchyma offers a thick barrier to local spread if the primary growth originates within the intrarenal portion of the pelvis and, as Jewett and others have so ably shown, the muscularis of the bladder offers a very significant barrier to tumor spread. It is little wonder, then, that neoplasms of the same degree of malignancy which arise in the ureter offer a much worse prognosis than those arising primarily in the intrarenal portion of the pelvis or in the bladder. A great many factors which vary from one case to another obviously influence the prognosis profoundly. The presence of local spread or distant metastasis at the time of operation presents a hopeless prognosis. There is almost universal agreement that complete nephroureterectomy with excision of a cuff of the bladder is the treatment of choice for all primary transitional cell tumors of the renal pelvis and ureter, and to leave behind even as little as the intramural segment of the ureter affects the prognosis adversely. Partial removal of the ureter is frequently done however, and often for quite justifiable reasons such as poor condition of the patient, technical operative difficulties, and others. Certain factors of operative technique must also be taken into account in considering prognosis. Spillage of tumor contaminated urine into the operative wound may lead to local recurrence. Excessive manipulation of the kidney or ureter may predispose to miliary spread.

In summary then, it would appear that the prognosis of squamous cell carcinoma of the renal pelvis remains hopeless. Transitional cell carcinoma of the ureter which has invaded through the ureteral wall presents an almost equally bleak outlook. On the other hand, benign tumors of the ureter or renal pelvis or those cases of superficial malignancy which are still confined to the mucosa have a very good prognosis if treated by nephroureterectomy. Even here, however, recurrences in the bladder are common and their early detection calls for periodic cystoscopic checkups. Although the prognosis of transitional cell carcinoma of the renal pelvis is bad, it is still better than that of a similar tumor arising in the

ureter primarily because of the mechanical barrier to spread offered by the renal parenchyma.

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DISCUSSION

DR. LOUIS M. ORR (Orlando, Fla.): I just want to commend these four essayists on their very splendid contributions. To me, Ormond Culp sounded just like the old days in Europe when he was about to sell the British a bill of goods. Oftentimes he did sell that bill of goods.

I would like to depart from science for a moment and tell a story. This is a story I think important enough to bring up to you inasmuch as it relates to the diagnosis of intrarenal tumors, pelvic tumors. In going back through our records, I find that in 29 years, we have had three instances of mature adult kidneys which have retained their fetal lobulations, and give the exact picture of an intrarenal tumor. Now this last and most unfortunate incident which occurred to us and made us all very unhappy took place while I was on the West Coast last year.

It goes this way: In 1953, a nurse came to our office complaining of an injury to her right kidney. She had hematuria. I performed the diagnostic procedures and sent back a report to her referring physician, also her employer, that I could find nothing unusual.

In a few weeks, during my absence, she returned to my office; one of my associates carried out pyelography by the retrograde method, and made a diagnosis of intrapelvic tumor. Hematuria was found to come from that kidney.

This was followed by the advice to have a nephroureterectomy at once. This operation was carried out. The woman made an uneventful recovery. The pathologist reported no renal tumor, but an aberrant artery circumscribing the pelvis which added to the lobulation and gave the exact picture that Dr. Vincent O'Conor showed of that upper pelvic area.

We were served just a short time ago, despite my absence from the city, by a member of the Sheriff's Department, with three summonses, suit for $125,000 on removing a kidney from a woman upon whom no biopsy had been taken.

Of course, this has disturbed me no end and would disturb you gentlemen if you were in the same situation. It was done by an associate, not by a partner. Its medico-legal aspects, which I will relate to you, are most interesting.

They brought suit on the basis of an individual performing an operation upon a patient whom they said had a normal kidney, and no biopsy had been taken. I have always been very loathe to perform biopsies, I think Dr. Henry Weyrauch will agree with me, on intrapelvic tumors. I think it is a very dangerous procedure. He showed in his excellent work some years ago, published in 1952, that you could do, with radioisotopes, a fairly safe renal biopsy of parenchymal tumors.

Here is the way the thing has now developed. We are being sued, all the people in the office involved in the operation of our business at a local address. The individual surgeon is being sued separately; so we are mixed up in this thing from a standpoint of people who operate offices and have assistants, associates, partners, or members of a clinic, in such a way that we are all being held for something I was not even present for at the time of the operation.

The individual himself is being sued jointly and doubly.

Every urologist who has seen this patient and who made pyelograms before the operation agreed that this was an intrapelvic tumor and that a nephroureterectomy should be performed.

The courts are holding at this time that any patient who has normal organs removed from the body should have been entitled to a biopsy, and that is the legal angle of all these things. I have never heard of anything quite like it before, but that is the situation as of this moment.

I couldn't bring you a lantern slide of this patient to show you her 1953 pyelograms, or her 1954 pyelograms, because they have been impounded by the court. But this is interesting, and I would advise all of you to carefully examine your insurance. There is no moral to it, except to be careful.

DR. J. A. C. COLSTON (Baltimore, Md.): I, too, want to express my great appreciation for the presentation of this very interesting subject, which has certainly covered every angle from diagnosis on to prognosis.

As far as prognosis is concerned, I would like to make a brief report on a case which I presented at the last meeting of this Association, simply to refresh the minds of those who are present, and also to present a brief abstract for those who were so unfortunate as to miss my presentation at the last meeting.

In brief, this was a lady who had a story of a hysterectomy 7 years previously, following which urinary drainage developed through the vagina, which gradually decreased and then stopped. That was on the right side, as was subsequently proven.

Hematuria then developed, and intravenous urograms and retrograde studies showed a definite filling defect in the pelvis of the left kidney and no secretion from the right kidney, so that we were faced with the pretty definite diagnosis of papillary carcinoma in the only remaining kidney.

She had been told at home that cancer had developed in her remaining kidney and there was nothing to do about it. I decided to expose this kidney in the vain hope that a small tumor might be present, which we might be able to excise. Fortunately, the kidney was very easily mobilized and brought up. She had an extrarenal pelvis. The pelvis was opened and a raspberry-sized papillary tumor protruded. The pedicle was up in the middle calyx, but we were able to excise a portion of the pelvis surrounding this pedicle, and then there was another smaller tumor we could not excise. It was too far up in the calyx. This was destroyed by electrocoagulation, and then we applied podophyllin, which has been demonstrated as a powerful toxic agent for epithelial cells. Whether this drug has had anything to do with the ultimate result is uncertain.

She has gotten along very, very well. Subsequent pyelograms, the last one 4½ months ago, and 4½ years after operation, show no filling defect. She has no symptoms.

It is interesting, however, that 2 years ago she returned with a mass on the right side. This was the side that had no function. This was explored transperitoneally; whereas at the first examination that right kidney was not palpable, now she had an easily palpable mass. A large cystic mass with hydronephrosis, with bluish contents in it, was removed. On examination of the mass, we found

a totally destroyed kidney, and in the greatly dilated pelvis there was growing a second papillary carcinoma.

This case, of course, is not presented in any way using the word "cure," but it is interesting from two standpoints, because it is a case of papillary carcinoma, bilateral, and we were unable to find a similar case in the American literature; also, a case of operation on a papillary carcinoma occurring in a single functioning kidney following which, so far, the patient has been clinically well.

Ferris and Daut reported a case which was operated on under similar circumstances, and they were able to excise a tumor of the pelvis, and this patient lived 7 years, dying ultimately in uremia. I think Dr. Tom Gibson has had a similar case of bilateral papillary carcinoma. Of course, this is a museum rarity, and the only reason I reported it last year, and am re-emphasizing it again, is the fact that if a diagnosis of tumor is made in a solitary kidney, one should not throw up one's hands, but should proceed to explore that kidney in the hope that he will find a situation and be as lucky as I have been, so far.

PARTIAL CYSTECTOMY FOR THE HYPOTONIC BLADDER: REPORT OF ELEVEN CASES

C. D. CREEVY

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Normal micturition involves four factors: expulsive force, opening of the internal meatus by the trigone, an external sphincter capable of relaxing, and a patent urethra. Normal expulsive force implies a normally innervated detrusor which responds to critical filling by complete emptying. Since diagnosis and treatment of mechanical obstruction to urination yield satisfactory results, urethral patency will not be discussed. By contrast the recognition, and particularly the correction, of reduced expulsive force may be difficult or impossible.

Four types of disorders weaken the detrusor. The first, neurogenic vesical dysfunction, may be central or peripheral, sensory or motor. Excluding trauma, the commonest variety probably results from an incomplete destruction or congenital deficiency of cells or fibers for vesical sensation in the spinal cord, peripheral nerves, or vesical plexus. Impaired sensation leads to chronic vesical distension which so interferes with venous return as to render the detrusor hypoxic. This causes hypotonia and later atrophy of the detrusor, i.e., impaired expulsive force. Included in this group is the hypotonic bladder sometimes associated with megaloureters. Swenson et al. attribute this to scarcity of ganglia in the vesical plexus; Powell calls it "megalobladder."

The second is neglected mechanical obstruction, exerting the same effect upon the detrusor as sensory neurogenic dysfunction. Relief of obstruction is curative unless advanced atrophy prevents effective contraction. Hermann, and Crabtree and Muellner have attributed this to a patchy replacement of detrusor fibers by fibrous tissue.

Third, excision of the rectum may, according to Campbell, cause sufficient pericystitis with edema of the detrusor to impair expulsion of the urine.

Last is reduced expulsive force of unknown origin, usually called "atonic bladder." Since such bladders do exhibit reduced rather than absent expulsive force, the term "hypotonia" is more accurate. In 1908 Shattock likened it to idiopathic dilatation of the esophagus, stomach, and colon. A year later Asch, reporting 11 cases, suggested disease of the vesical nerves or ganglia as a cause, while Thomson-Walker spoke of a lesion of a "sympathetic reflex center" in the hypogastric and hemorrhoidal plexuses. Geraghty (1917) suspected a peripheral neuritis. Kretschmer and Heckel reviewed the whole subject in 1932. Houtappel has recently postulated a defect in the detrusor fibers themselves.

Commoner in the female, primary hypotonia causes increased frequency and difficulty of urination with considerable residual urine without complete retention; it probably begins with unnoticed, infrequent micturition. Psychiatric and neurological disorders and mechanical obstruction are absent. Capacity is large, expulsive force is reduced, trabeculation is minimal or absent, and there are no

diverticula large enough to contain the residual urine. Sensation is intact. A complicating cystitis may overshadow the underlying cause. The upper tract is normal, since intravesical pressure is low. Diagnosis is made by exclusion.

TREATMENT OF PRIMARY HYPOTONIA

While residual urine is still small, complete emptying may be achieved with cholinergic drugs, urination at regular intervals in two or more stages, and manual suprapubic pressure. If this regimen fails, the internal sphincter may be weakened by transurethral resection. However, these patients are rarely seen by the urologist until residual urines are large, when conservative measures, as well as transurethral resection, usually fail.

Since the hypotonic bladder can expell a considerable volume, it should be possible to eliminate residual urine by reducing vesical capacity. Because the vesical nerves ramify from a plexus beneath the trigone, and most of the blood vessels come from behind and laterally, one may remove the vertex with portions of the contiguous walls without damaging the remaining bladder. This was apparently done first by Orr in 1937, and later by Crabtree and Muellner, by Fish, and by Houtappel. Together they have reported 24 cases, mainly of neglected mechanical obstruction, with fairly uniform improvement. In order to secure consistent results, I have resected enough of the dome of the bladder so that the remnant can be sutured snugly about a Kearns balloon inflated to 300 cc and subsequently withdrawn; wedge excision of the posterior lip of the vesical orifice with transverse suture is usually done as well. Cystostomy is maintained for two weeks thereafter.

CASE REPORTS

Case 1. Mrs. K. B., aged 32, University Hospital No. 850716, had always urinated frequently, and was told in 1947 that she had a large residual urine, although no treatment was suggested. Once, after removal of 2 liters of residual urine, she did not urinate for 36 hours. Retrograde pyelograms in August 1952 were normal, and a cystogram showed a large, nontrabeculated bladder. She had had 2 cesarian sections.

In September 1952, residual urine measured 1500 cc, and capacity was 2000 cc. The urethra, ureteral orifices, and bladder were otherwise normal except for poor expulsive force. Neurological and serological examinations yielded normal results.

At operation on October 30, 1952, the internal urinary meatus felt normal and the bladder was normal except for its size. Partial cystectomy was done, and she was discharged 16 days later without residual urine.

She had no complaints whatever referable to her bladder until March 1955 when, following recovery from division of adhesive bands for acute intestinal obstruction, she felt that she was again retaining urine. On March 22, 1955, an excretory urogram was normal but there were 785 cc residual urine. An inlying catheter was inserted, but she again suffered acute intestinal obstruction; 10 days after operation she began to empty her bladder completely.

Case 2. Mrs. E. L., aged 44, No. 645918, had poliomyelitis in childhood, but difficult urination did not appear for many years. Transurethral resection and urethral dilatations then failed, and overflow incontinence appeared shortly before admission. The only positive finding on general, neurological and serological examination was slight weakness in one upper extremity. There were 450 cc clear residual urine, and the upper tract was normal. At cystoscopy the urethral aspect of the internal meatus was scarred but flexible and open. Mild cystitis was present with a capacity of 1100 cc. On January 5, 1953, plastic widening of the internal urinary meatus and partial cystectomy were done. She was discharged on the sixteenth postoperative day without residual urine.

On March 7, 1955, 26 months later, she was voiding somewhat more often than normal. The internal meatus was unchanged; there was mild cystitis with a capacity of 500 cc, and 30 cc of clear residual urine containing Bacillus proteus. This is being treated.

Case 3. Mrs. L. A., aged 44, No. 875683, had symptoms of obstruction to urination for several years. A month before admission dysuria and pyuria appeared, and her physician found residual urines ranging from 250 to 350 cc. Antibiotics relieved the irritation, but cholinergic drugs and urethral dilatations did not reduce the residual urine. The kidneys were normal.

On October 11, 1954 the urethra was normal. The bladder was large and faintly trabeculated, and expulsive force was poor. Cystogram (fig. 1) showed only a large bladder. Neurologic and serological examinations yielded normal results. At operation on October 13, 1954, the bladder was large and thin walled.

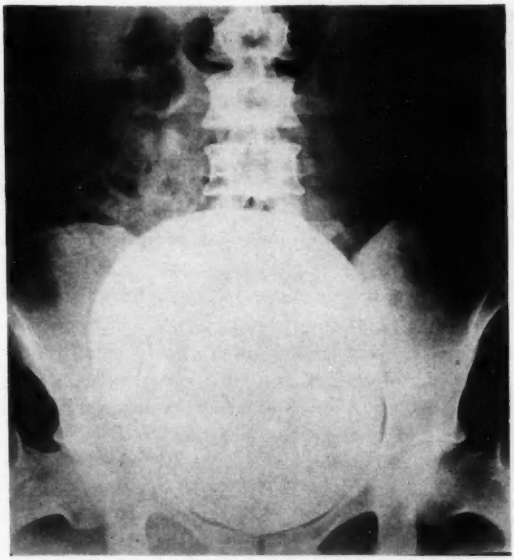

FIG. 1. Case 3. Cystogram of primary hypotonia

The internal meatus admitted the forefinger. Therapy was like that in case 2. She was dismissed on the seventeenth postoperative day urinating normally without residual urine. On May 4, 1955, seven months after operation, she was asymptomatic; her physician found 10 cc clear residual urine containing Escherichia coli.

Case 4. Mrs. V. G., aged 67, No. 871811, complained of urinary obstruction increasing in severity for several years. She was a rather neurotic widow with essential hypertension.

On admission there were 190 cc sterile residua[1] urine. Excretory urography and neurological as well as serological examination yielded normal results. The urethra, ureteral orifices, and bladder were normal except for a vesical capacity of 800 cc with impaired expulsive force.

Operation on June 24, 1954 was identical with that in cases 2 and 3. When the suprapubic tube was clamped on the fourteenth day, she voided normally. When it was withdrawn, she was completely incontinent without residual urine. Cystoscopy disclosed no cause for the incontinence. Houtappel commented upon the frequency of partial incontinence in his postoperative patients. She was discharged with an inlying catheter on the twenty-first postoperative day to the care of her physician. Three months later he reported that the residual urine was 60 cubic centimeters "an hour after voiding."

Nine months after operation she wrote that she was getting up once at night with normal diurnal frequency; long postponement occasionally caused incontinence. The end result is good, but convalescence was slow and unpleasant.

Here are 4 women ranging in age from 32 to 67 with large residual urines without neurological disorders or mechanical obstruction to urination. Their disorder is probably best called primary hypotonia of the bladder. All responded well to partial cystectomy. While this was supplemented in three by plastic widening of the vesical neck, cystoscopic evidence indicated that this was unnecessary, and it was done to avoid subsequent operations if possible. None of the patients has significant residual urine 7 to 27 months after operation. One remained well for 30 months, then relapsed after an operation for acute intestinal obstruction. This is not surprising, since the detrusor fibers of these people are probably inherently abnormal. However, she subsequently recovered her ability to empty the bladder.

In the presence of complete retention, one must be wary of neurological and psychiatric disorders before blaming primary hypotonia, as illustrated by case 5. Sister C. S., a nun aged 27, No. 871088, had difficult urination for 2 years. During the month preceding admission, she had several attacks of acute retention with volumes up to 1500 cc. Use of cholinergic drugs with intermittent and inlying catheterization had been futile.

The residual urine on admission measured 400 cc. General and serological examinations were not informative. The neurological consultant suspected multiple sclerosis but could not prove it. There was spina bifida occulta of the first sacral vertebra. The upper urinary tract, the spinal fluid, its pressure, and a spinogram were normal. The cystogram showed a large, nontrabeculated bladder.

Cystoscopy disclosed no abnormality except a capacity of 900 cc with impaired expulsive force but normal sensation. Cholinergic drugs, suprapubic pressure, two-stage urination, and catheterization did not induce normal urination.

On June 10, 1954, plastic widening of the internal meatus and partial cystectomy were done. She was discharged without residual urine on the twenty-first postoperative day. Within a week the residual urine reached 500 cc. Intermittent catheterization and cholinergic drugs failed. She was readmitted on September 21; nothing abnormal was noted at cystoscopy. The neurologic findings were unchanged. Transurethral resection of the internal sphincter was done twice without benefit. Pudendal blocks with procaine were futile. Suprapubic cystostomy was re-established on October 5, 1954 and she was discharged on October 11.

On March 9, 1955 her physician reported that residual urine with the tube clamped was 250 cc, and that it fell to zero after a pudendal block with procaine. When this was repeated with saline, the result was the same.

It seems in retrospect that she has hysterical urinary retention based upon dissatisfaction with the ascetic life, and that psychiatric examination should have been made before operation was considered, but multiple sclerosis has not yet been excluded.

OTHER TYPES OF HYPOTONIA

Patients with other types of hypotonia may benefit from partial cystectomy. In *case 6*, residual urine persisted after complete removal of *mechanical obstruction*. Master D. P., aged 4, No. 784087, had always had a large abdomen, pyuria, and frequent, dribbling urination. The abdominal muscles were absent; intestinal peristalsis was visible. There were 600 cc cloudy residual urine, and urography showed a much dilated solitary left kidney and ureter (fig. 2, *A*) with a large bladder containing 2 small diverticula at the vertex (fig. 2, *B*). Cystoscopic examination disclosed a contracture of the vesical neck with a large, untrabeculated bladder having poor expulsive force.

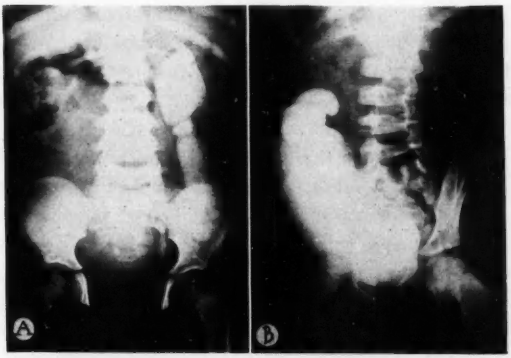

FIG. 2. Case 6. *A*, urogram in congenital absence of abdominal muscles. *B*, cystogram

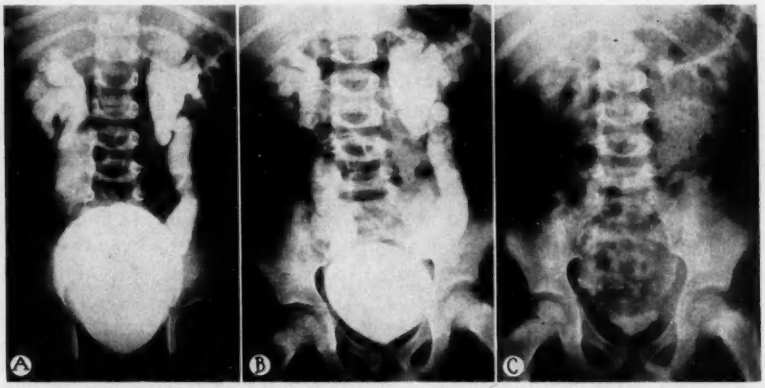

FIG. 3. Case 7. *A*, congenital megalobladder with reflux before operation. *B*, cystogram in same patient 6 months after partial cystectomy. *C*, after three consecutive urinations.

Transurethral resection reduced the residual to 150 cc. On January 27, 1948 about one-third of the wall of the bladder, including the 2 diverticula, was excised, with primary closure. No abdominal muscles were found. He was discharged 2 weeks later without residual urine. His father refused to bring him back but wrote, 7¼ years after operation, that he had remained perfectly well, and enclosed a photograph of a robust boy of 11. An excretory urogram made in July 1955 through the courtesy of Dr. P. J. Steiner of Lemmon, South Dakota showed that the upper urinary tract had not changed since his original admission nearly eight years ago.

Congenital ureterectasis has been mentioned, and is illustrated by *case 7*. Master P. L., aged 6, No. 869333, had always had pyuria with bouts of chills and fever. Another cystoscopist had said that he had bilateral hydronephrosis from obstruction at the vesical neck. Upon admission 2 days later he had a fever of 104F, a urea nitrogen of 50, and 450 cubic centimeters of turbid residual urine containing Aerobacter aerogenes. With antibiotics and an inlying catheter the temperature and urea nitrogen returned to normal. Cystography then outlined a large, smooth bladder with reflux delineating grade 3 bilateral hydronephrosis with correspondingly dilated ureters (fig. 3, *A*). At cystoscopy the internal meatus gaped, the ureteral orifices were dilated, the bladder was not trabeculated, and expulsive force was poor.

After continuous suprapubic drainage for 3 months, a cystogram showed no improvement of the bladder but the upper tract had improved a trifle. At operation on June 24, 1954, the detrusor was thick and pale without evidence of contractility, and the internal meatus stood open. Wedge excision and transverse closure of the posterior lip of the internal meatus, and partial cystectomy were performed. Cystostomy was continued for a month, after which timed two-stage urination, manual suprapubic pressure, and very small doses of antibiotics were instituted.

In January 1955, the clear residual urine measured 30 cc. Cystography showed

a smaller bladder with reflux (fig. 3, *B*). The upper tract was unchanged. Stephens' regimen was then tried: roentgenography after micturition showed about one-half of the contrast agent in the upper tract; a second effort removed about half of it; a third attempt almost emptied the kidneys (fig. 3, *C*). His mother was instructed to have him void 3 times with suprapubic pressure at each sitting, every three hours during the day, and once at night. He was reported well in April 1955.

Experience suggests that partial cystectomy is applicable to other types of neurogenic dysfunction only if there is sufficient sensation to permit active cooperation in emptying the bladder. *Cases 8* and *9* are pertinent. Two girls, T. M., aged 12, hospital No. 755751, and M. M., aged 8, hospital No. 755681, had overflow incontinence following operations early in life for meningomyelocele, and both had large bladders with advanced bilateral hydronephroses. Each had futile trials of cholinergic drugs, urination by the clock, suprapubic manual pressure and, finally, transurethral resection. Partial cystectomy reduced the residual urine from 200 to as low as 30 cc in T. M., but she is still incontinent. The low residual justifies procrastination; if improvement does not occur, diversion of the urine through an isolated ileal loop (Bricker) may be considered. The other patient was freed of residual urine for a brief period, only to relapse. Bricker's operation was then done because of progressive hydronephrosis.

When the patient has enough sensation to permit him to help himself, results are better, as in *case 10*. G. M., No. 655609, a man of 60, had "infantile paralysis" in childhood and had been incontinent of urine until 1935, when reduced sensation to pinprick and light touch was found below T 11, indicating that his original illness was a transverse myelitis. Transurethral resection yielded complete relief until 1952 (17 years), when small stream, hesitancy, straining, and urinary incontinence recurred.

On readmission in July, his neurologic status was unchanged. The prostatic urethra was well resected and smooth; the residual urine was 150 cc and sterile. The bladder was trabeculated and held 700 cc.

Suspecting a hypotonic detrusor from the old neurogenic lesion, trocar cystostomy was established for 3 months. The tube was then clamped, but residual urine was the same. About one-third of the bladder was removed in October 1952, and he was discharged 2 weeks later without residual urine. He reported in March 1955, 29 months after operation, that improvement had persisted, but that he still had intermittent incontinence.

Case 11. Mrs. C. F., aged 69, No. 812750, had mild neuropathy secondary to diabetes of 26 years' duration. Urinary infection had recurred and relapsed for years, and transurethral resections in 1951 were ineffective. In April 1954 she had a nontrabeculated bladder with a capacity of 1200 and a residual of 450 cc containing Aerobacter aerogenes. There was no urethral obstruction. Partial cystectomy was done. Eleven months later there were 90 cc infected residual urine, but capacity was now 550 cc, and the upper urinary tract was normal. Antibiotics had not influenced the infection.

Comment. Objective has greatly exceeded subjective improvement; the pronounced reduction in both residual urine and capacity seem worthwhile.

PATHOLOGIC FINDINGS

There were no consistent histological changes in the bladder by which the nature of the complaint could be identified. There was evidence of infection in the mucosa and submucosa in most instances, but the muscularis appeared normal, even in the patient in whom it seemed pale and fibrous at operation.

SUMMARY AND CONCLUSIONS

Eleven patients have had partial cystectomy to eliminate residual urine from loss of expulsive force in the absence of mechanical obstruction. The capacity of the bladder was reduced to 300 cc, and cystostomy was maintained for 2 weeks. In all but two, plastic widening of the internal sphincter was also done. For convenience the types of lesions and results have been classified as follows:

Group I Primary hypotonia
- A. Psychologically and neurologically normal: 4 cases, 4 cures. (One patient relapsed after operation for acute intestinal obstruction 30 months after partial cystectomy.)

Group II Hysterical urination retention?
- Psychoneurotic with questionable neurological findings (multiple sclerosis?): 1 case, failure.

Group III Mechanical obstruction
- Psychologically and neurologically normal. Residual persisting despite relief of obstruction: 1 case, 1 cure.

Group IV Neurogenic vesical dysfunction
- Psychologically normal; lesion of nervous system
- A. Megalobladder and ureters: 1 case, great improvement.
- B. Myelodysplasia with anesthesia of bladder: 2 cases, 2 failures.
- C. Minimal old transverse myelitis: 1 case, improved (residual absent, but other symptoms).
- D. Diabetic neuropathy: 1 case, much improved.

From these data one may conclude that partial cystectomy will eliminate or greatly reduce residual urine in the presence of a hypotonic bladder if:

1) There is no psychiatric cause of urinary retention
2) The sensory nerve supply is not hopelessly deficient
3) Mechanical obstruction is absent.

In primary hypotonia and in neurogenic vesical dysfunction, the inherently defective detrusor may decompensate again after partial cystectomy if subjected to severe stress.

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ILEAL LOOP DIVERSION: ITS APPLICATION TO THE TREATMENT OF NEUROGENIC BLADDER DYSFUNCTION

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Most patients with neurogenic bladder dysfunction from any cause may be treated conservatively by conditioning, transurethral resection of the bladder neck, pudendal neurectomy, or occasional sacral neurectomy. There are individuals, however, with upper motor neuron lesions who experience such unsatisfactory reflex bladder function that it is impossible to keep them dry. Other patients with lower motor neuron lesions, in spite of fairly satisfactory voiding, probably because of lack of normal accommodation to filling and constantly high bladder pressure, suffer reflux and upper urinary tract complications of pyelonephritis, calculi, and hydronephrotic atrophy.

Male patients may be satisfactorily treated by indwelling catheter or condom drainage after resection of the bladder neck or other procedures that have not corrected the situation. Female patients, however, present a serious problem of urine collection because of leakage about the catheter. No satisfactory mechanism has been devised to collect urine from the incontinent female.

Permanent cystostomy and vesical neck exclusion would appear to be the simplest procedure, but as in one of the cases to be presented it did not solve the problem. Some other type of urinary diversion becomes necessary. Ureteroenterostomy to the intact sigmoid is out of the question because of upper urinary tract damage and rectal incontinence. Cutaneous ureterostomy or nephrostomy is fraught with troubles and almost always results in gradually impaired renal function due to persistent infection, calculus formation and difficulty in reintroducing tubes which often necessitate re-operation. Free drainage diversion without tubes or catheters would seem to be the solution.

We have, therefore, elected to try urinary diversion in selected cases by fashioning a free-draining ileal loop into which the ureters have been transplanted using a direct end-to-side anastomosis essentially as described by Bricker.[1, 2] Recently, Hansen, Eggers, Bill, and Dillard[3] reported the use of this procedure in the treatment of urinary incontinence in two patients with congenital abnormalities—exstrophy and myelomeningocele. The method has been used by us in the treatment of 4 patients. These cases are presented not only to illustrate use of this particular technique but to call attention to the problems involved in treating this type of patient. Urine collection has been best accomplished by the use of the Rutzen bag. By and large, this has proved satisfactory.

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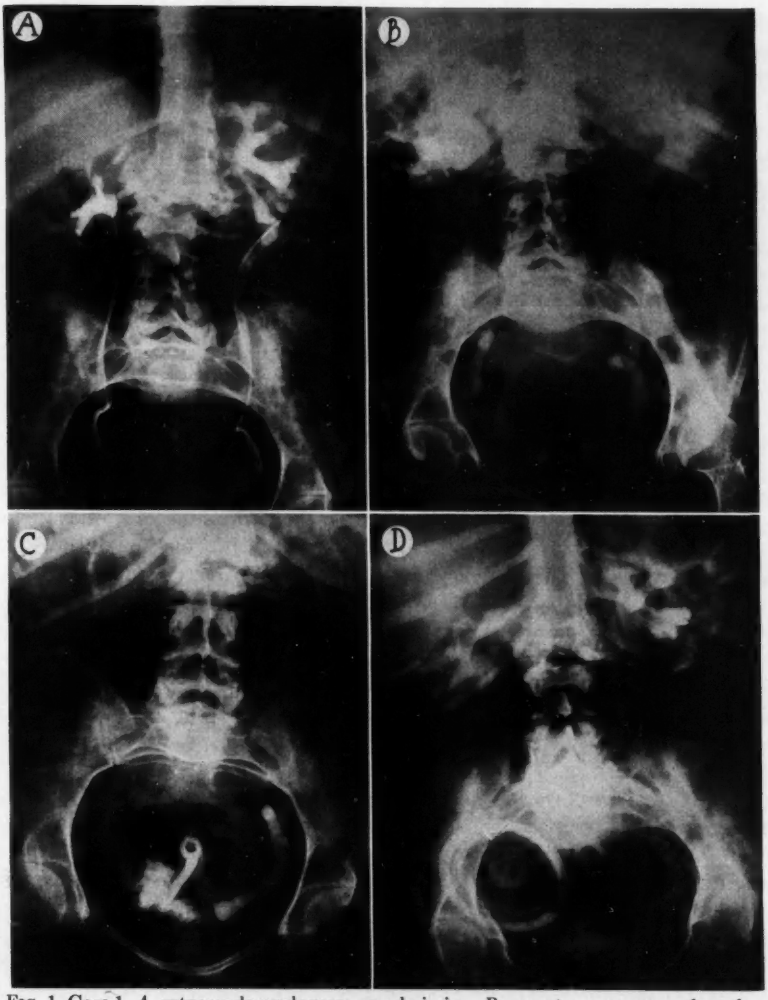

FIG. 1. Case 1. *A*, retrograde pyelogram on admission. *B*, excretory urogram after closure of vesical neck and suprapubic cystostomy (3-hour film). Note degree of hydroureter and hydronephrosis. *C*, injection of dye into bladder through suprapubic tube to demonstrate reflux into ureters. *D*, excretory urogram 5 months after ideal loop procedure. Marked improvement in appearance of renal pelves is apparent.

CASE REPORTS

Case 1. M. J., M.G.H. No. 866571. A 25-year-old female paraplegic was admitted to the Massachusetts General Hospital in July 1954 for rehabilitation. Eight years prior to admission she had fallen and suffered a back injury resulting in complete paralysis below the the T10 segment. Laminectomy was done, but

there was no return of sensation or motor power. She spent 2 years in another hospital where attempts at bladder conditioning were unsuccessful. Catheter drainage was complicated by the development of a vesico-urethro-vaginal fistula which made urine collection impossible. Continuous wetness resulted in numerous ulcers over the sacrum and about the perineum and upper thighs for which various plastic procedures had been carried out. For some time no effort at all had been made to collect urine.

Physical examination revealed a thin, complaining, odiferous patient who appeared chronically ill. There were multiple scars and ulcers about the perineum, upper thighs and over the sacrum. A vesicovaginal fistula was palpated 1½ inches in diameter involving the bladder neck. There was complete paralysis and complete loss of sensation below the umbilicus.

Laboratory studies showed anemia, normal blood chemistry values, and many white blood cells in the urine. An intravenous urogram and retrograde pyelogram showed good kidney function and changes suggestive of chronic pyelonephritis (fig. 1, *A*). Cystoscopy confirmed the size and location of the vesicovaginal fistula. It appeared that the floor of the bladder neck and urethra had sloughed.

Before any attempt could be made to treat the various ulcers it was apparent that some form of urinary diversion was necessary. Therefore, on July 28, 1954 the bladder neck was divided, separated from the vagina, closed, and a cystostomy established. Following this procedure the suprapubic tube drained well. The vaginal leakage disappeared. Many of the ulcers about the perineum and over the sacrum healed. However, intravenous urograms showed progressive bilateral hydroureter and hydronephrosis and impairment of renal function (fig. 1, *B*). It was at first thought that ureteral obstruction had developed as a result of trauma incident to dissecting up the bladder neck or to periureteritis, but a cystogram (fig. 1, *C*) demonstrated reflux from the bladder into both ureters. It was therefore concluded that damage to the parasympathetic nerves had occurred as a result of disturbance of the floor of the bladder which somehow affected delivery of urine to the bladder. At any rate, the presence of pyelonephritis and rapidly failing renal function made further diversion necessary. After discussing the pros and cons of cutaneous ureterostomy and nephrostomy, since ureterosigmoidostomy was out of the question, it was decided to fashion an ileal loop. This was done on September 17, 1954. At that time no obstruction could be demonstrated in either lower ureter. Cystectomy was done at the same time to eliminate an otherwise chronically infected pouch. Her postoperative period was somewhat stormy but ultimate recovery was good and renal function has returned to a surprising degree. A recent excretory urogram is shown in figure 1, *D*. There is slight residual hydronephrosis, particularly on the left. No attacks of pyelonephritis have occurred. The sacral ulcers are being treated and are responding well. Patient is undergoing rehabilitation with braces.

Case 2. M. W., M.G.H. No. 306555. A 38-year-old nurse was first seen by one of us (W. F. L.) in October 1948. In 1938 operation for herniated lumbar intervertebral disc was done. Pain continued thereafter and 4 years later first a uni-

lateral and then bilateral chordotomy was done. The result of these procedures was unsatisfactory in that only spotty anesthesia was present, moderate weakness of muscles in both lower extremities developed, and worst of all a spastic reflex bladder and rectal incontinence developed.

Study in the hospital showed a normal upper urinary tract and spastic reflex bladder with maximum capacity of 80 cc. Voiding of 30 to 50 cc occurred frequently and irregularly. Tidal drainage did not modify bladder function. The patient was discharged to use an indwelling catheter at night so that she could sleep undisturbed. It became evident that this was no solution to the problem so that patient was readmitted to the hospital for further study. Cystometric study was done after blocking the sacral nerves which showed immediate improvement in vesical capacity, absence of reflex activity until near normal capacity was reached. Therefore, on January 24, 1949, through a low abdominal incision, the pelvis was explored and part of the parasympathetic nerve supply to the right side of the bladder was divided. Change in bladder function was quite remarkable in that she could hold urine for two to three hours and voided 150 cc urine each time. Residual urine was less than 100 cc.

The effect of this procedure was short-lived in that by July 1949 she was voiding as frequently as before and bladder capacity was 100 cc or less. Her condition gradually reverted to that before operation. Therefore, in November 1949 the patient was readmitted to the hospital. Cystometric studies before and after novocain block of the sacral nerves demonstrated reversion from reflex irritable bladder with capacity of 90 cc to capacity of 400 cc without reflex activity. Furthermore, after block the patient was able to void without difficulty. Excretory urograms were again normal. On the basis of this the patient was operated on again November 7, 1949 through a midline incision. After identification of the second, third and fourth sacral nerves deep in the pelvis behind the hypogastric vessels, rami were found passing to the bladder pedicles, all of which were sectioned and portions removed. After operation patient's urinary function became almost normal. Cystometric study showed capacity of 250 cc with slight tendency to hypertonicity. The patient was completely continent and voided from 150 to 200 cc each time. Over a period of 1 year her bladder function gradually deteriorated again, bladder capacity diminished, frequency recurred, and stress incontinence became troublesome. Finally, since the patient was working, she was placed on constant catheter drainage.

She was readmitted on March 16, 1951 with acute right pyelonephritis. Excretory urograms were again normal. Bladder capacity was found to be 100 cc again. Block of sacral nerves at this time showed no effect on bladder function indicating that there had been no regrowth of parasympathetic nerves. The patient was miserable on catheter drainage so that suprapubic cystostomy was done on March 29, 1952. This did not prevent urethral leakage and made the patient uncomfortable. On September 23, 1952 this was closed and urethral catheter drainage reinstituted. The situation became intolerable because of leakage about the catheter and encrustation.

Therefore, the patient was readmitted on June 17, 1953 and after considerable

discussion it was felt that enlargement of the bladder might help, and on June 23, 1953 an ileo-ascending colostomy and transplantation of the cecum to the vertex of the bladder were done without difficulty. Convalescence was easy. The patient voided well in 200 and 300 cc amounts. Residual urine was 50 cc.

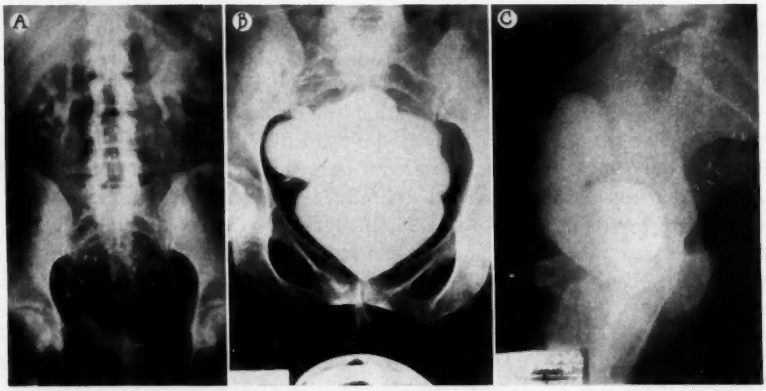

FIG. 2. Case 2. *A*, excretory urogram, November 1949. *B*, cystogram after bladder enlargement using cecum. Note reflux into right lower ureter. *C*, oblique cystogram after bladder operation.

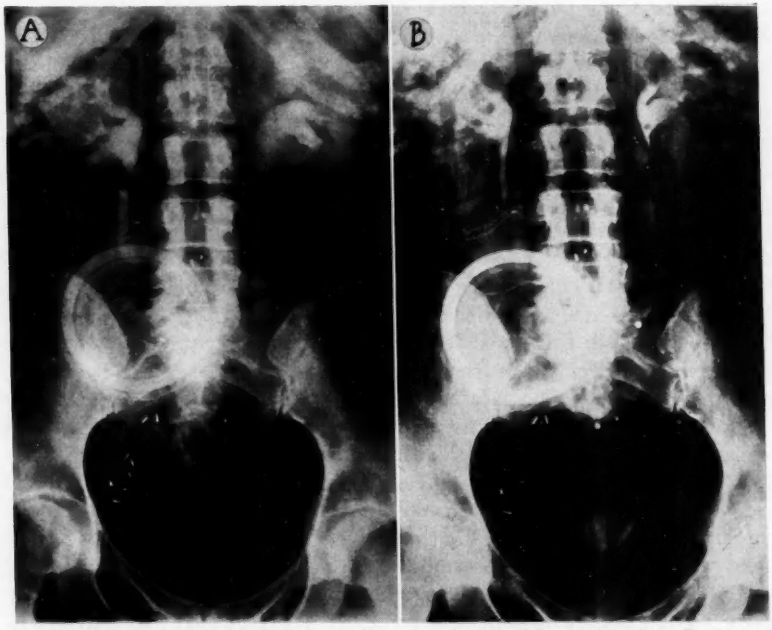

FIG. 3. Case 2. *A*, excretory urogram 2 weeks after ileal loop diversion. *B*, excretory urogram 4 months after ileal loop diversion.

The general condition improved markedly for a time after this. She gained weight and felt much improved. During the winter of 1953–54 she went to Florida. Pains in the right kidney area developed associated with fever which seemed to be due to pyelonephritis. When she returned to Boston in the spring of 1954 it was obvious that she was not doing well. There was between 100 to 200 cc of residual urine. Excretory urograms showed a normal upper urinary tract, but a cystogram showed reflux up the right ureter which undoubtedly explained the attacks of pyelonephritis. She was again put back on catheter drainage but this did not work well so that finally she was re-admitted to the hospital on October 5, 1954 and an ileal loop was fashioned into which both ureters were transplanted. Since that time she has done well. The cecal pouch was excised from the bladder which was left in place. Patient has had considerable irritation and some discharge from the bladder since indicating that a cystectomy should have been done.

Figure 2, *A* shows the urinary tract prior to bladder enlargement operation (1949). Figure 2, *B* and *C* are the cystograms after the cecal pouch was set into the bladder. Figure 3, *A* is an excretory urogram 10 days after ileal loop procedure. Figure 3, *B* is an excretory urogram 4 months after operation.

*Case 3.*V. P., Roger Williams Hospital No. 550432. A 50-year-old woman was first seen by W. F. L. in 1938. At that time she had a history of frequency and suprapubic pain over an 8-year period treated by numerous urologists with only

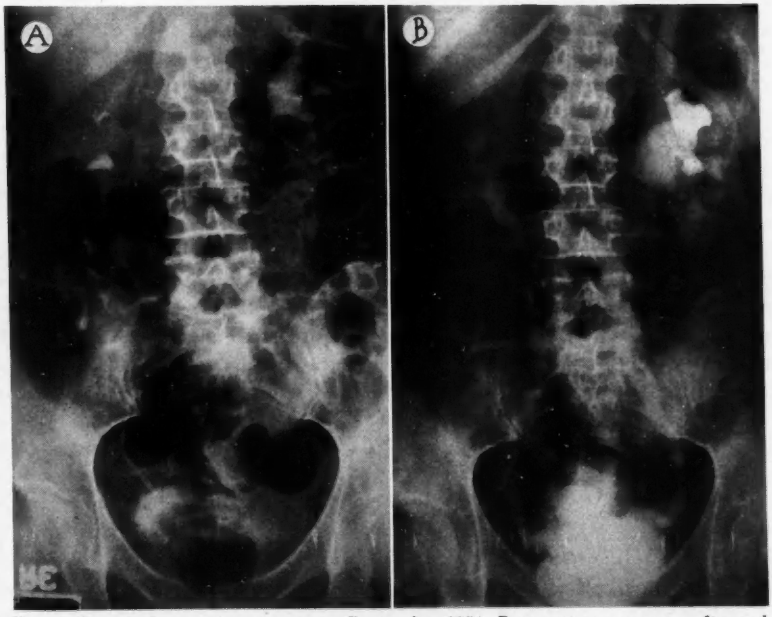

FIG. 4. Case 3. *A*, excretory urogram, September 1954. *B*, excretory urogram after pelvic neurectomies.

temporary relief. Cystoscopy revealed three lesions characteristic of interstitial cystitis on the right side of the bladder. From then until the fall of 1954 the patient had had intermittent treatment with only partial or temporary relief. Finally, she was admitted to the Roger Williams Hospital in Providence, Rhode Island. Her surgeon felt that presacral neurectomy might help so this was performed removing not only the presacral nerves but lateral pelvic tissue which must have included at least a portion of the hypogastric plexus and the parasympathetic nerves, because afterward the patient was completely relieved of pain but voided with difficulty and began to have discomfort in both kidney regions associated with fever. Excretory urography, which had previously been normal (fig. 4, *A*), showed marked bilateral hydroureter and hydronephrosis (fig. 4, *B*). The senior author was called to see the patient at this time and recommended catheter drainage because of a large volume of residual urine and serious damage to the upper urinary tract. After an indwelling catheter had been placed the temperature gradually returned to normal and excretory urograms later showed improvement in the degree of hydroureter and hydronephrosis. It was apparent that the patient either had to be carried on catheter drainage, cystostomy, or some other form of urinary diversion. After discussion with the patient ileal loop diversion was decided upon and operation carried out on January 3, 1955. The bladder was removed at the same time. Convalescence was stormy with distention and vomiting. Finally, it became obvious that small bowel obstruction was present. Re-operation was carried out and a loop of small bowel found adherent to the base of the ileal loop. The patient died following this procedure. During the time patient lived there was never any difficulty with the collection of urine from the loop and patient was free of any indication of upper urinary tract complications.

Case 4. H. F., M.G.H. No. 716434. A 48-year-old married woman was first seen in May 1952 complaining of urinary incontinence. Twenty years previously radiation therapy had been given to a plantar wart on the sole of the left foot. The area never healed properly so that over the years treatment consisting of skin grafts, pedicle grafts, lumbar sympathectomy, and finally transmetatarsal amputation was done to get a usable foot. None of these procedures succeeded. Pain became a problem. Finally, unilateral chordotomy was done in 1951 with relief of pain. However, when the patient became active again the skin over the amputation stump broke down and pedicle graft again was tried but infection in and about the graft with ascending lymphangitis developed. Worst of all, after chordotomy, neurogenic bladder dysfunction developed so that patient dribbled urine frequently and carried 250 cc of residual urine. Even catheter drainage would not keep her dry since urine was frequently passed about the catheter. Attempts to modify bladder behavior by tidal drainage were unsuccessful. Cystoscopy showed nothing. Cystometric study demonstrated an extremely hyperactive reflex bladder.

Finally, the patient was admitted for study on December 22, 1952. Blocking of sacral nerves and studies of bladder function were done. These seemed to show that when the left sacral roots were blocked, function became more normal. Resection of the left parasympathetic nerves was done on December 24, 1952.

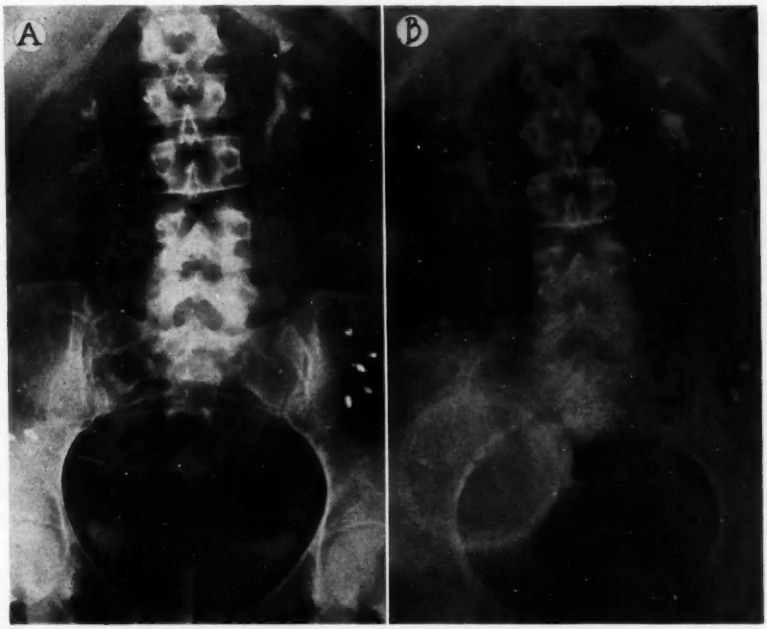

FIG. 5. Case 4. *A*, excretory urogram, February 1954. *B*, excretory urogram after ileal loop diversion.

The patient could not void after this and the only benefit derived was that she could stay dry on urethral catheter drainage. Neurological examination after this suggested an underlying disease such as multiple sclerosis. During the next 2 years she was carried along on indwelling catheter drainage. Attempts on several occasions to revert to normal voiding were unsuccessful.

During the spring of 1954 the skin over the left foot eroded, became infected and was associated with lymphangitis. This recurred each time activity was begun. Finally, amputation of the left leg below the knee was done and prosthesis fitted. So far, it appears that the skin of the stump will be able to withstand irritation of the artificial limb. Bladder drainage by catheter became completely unsatisfactory because of incrustation, leakage, and chronic irritation with bleeding. The patient was admitted for the last time in February 1955. Excretory urography (fig. 5, *A*) showed normal upper urinary tract. Cystoscopy revealed a contracted bladder with marked chronic inflammatory changes. An ileal loop into which both ureters were transplanted was fashioned and the bladder excised. The patient made a good recovery and for the first time in 5 years is comfortable and free from catheter and urine leakage. The postoperative excretory urogram is shown in figure 5, *B*.

DISCUSSION

One may justly criticize the handling of these cases, yet we are sure that anyone who has come to grips with rehabilitation of individuals afflicted with

this type of neurogenic bladder dysfunction will view our efforts with a certain amount of charity.

Our own analysis of the cases is somewhat as follows. The cystostomy and vesical neck exclusion performed on the first patient resulted in damage to parasympathetic nerves that should not have occurred. However, the defect in the bladder neck necessitated considerable dissection about the bladder base in order to effect closure of the fistula. The resulting ureteral reflux, hydroureter and hydronephrosis with rapidly diminishing renal function in the presence of a freely draining cystostomy tube is difficult to explain. Perhaps lower ureteral peristalsis was interrupted by nerve section or damage. One might have solved the problem by skin ureterostomies performed through pedicle flaps as described by Talbot et al.[4] Cystectomy would have been necessary to be rid of the chronically infected vesical pouch. We elected ileal loop diversion because it offered one stoma, freedom from catheters, and the hope of freer drainage. The result thus far after 9 months seems quite satisfactory.

The procedures utilized in treating the second patient seem poorly chosen and redundant. There seemed, however, to be good basis for denervation of the bladder. The utilization of two procedures was inexcusable, yet we were not familiar with the procedure and found no precedent to guide us. At last we developed a technique which allows denervation of the bladder without damage to the sacral nerve routes. This, in a patient without paraplegia, would have resulted in further weakness of pelvic girdle and leg muscles. Perhaps the subsequent contraction of the bladder may have been prevented if we had been aware that this would occur. Interval dilatation could have been tried. It was interesting to note that after denervation of the bladder its outline by cystogram was smooth and normal and the patient voided almost normally. Only small amounts of residual urine were present. This may be compared with the cystogram in case 3 after partial denervation of the bladder which shows marked irregularity and asymmetry. The use of the cecal pouch was a frank experiment which did not solve the problem because it decompensated. No hyperchloremia was noted. Repeated attacks of right pyelonephritis uncontrollable by medication, undoubtedly due to right ureteral reflux, forced us into some type of urinary diversion. Again ureterostomy seemed less satisfactory than the ileal loop which has worked well. The only remaining complaint is collection of purulent material in the bladder which is irritating and unpleasant. Cystectomy should have been done.

Patient 3 presented the same problem as patient 1 in that hydroureter, hydronephrosis and pyelonephritis rapidly followed partial denervation of the bladder. The bladder outlined by the cystogram shows a smooth, symmetrical vesical neck and base while the vertex is very irregular and asymmetrical. This suggests to us that the only remaining portion of the bladder normally innervated was the right half of the vertex. This same cystographic appearance was noted during the war (by W. F. L.) after partial cauda equina lesions resulting from wounds.

[4] Talbot, H. S., Paull, D. P. and Read, G. R.: Late complications of paraplegia III. Treatment of vesicoureteral reflux by skin ureterostomy through a pedicle flap. J. Urol., **70:** 216, 1953.

The question arises in regard to partial parasympathetic nerve lesions whether the part with deficient or absent innervation could be removed and leave a normally functioning bladder. This requires further investigation. This patient's death after release of intestinal obstruction was tragic. It simply points out one of the possible complications of the ileal loop operation which is occasionally bound to occur, must be watched for and corrected early. The loop functioned perfectly with no leak or ureteral obstruction. Perhaps we should have tried a longer period of catheter drainage and transurethral resection of the bladder neck but since bilateral reflux was present it seemed best to use a procedure which would solve the whole problem. Hutch's operation[5] would have corrected only one aspect of the problem.

The fourth patient presented problems similar to patient 2—unsatisfactory reflex bladder function after chordotomy and in the presence of intrinsic pyramidal tract disease (multiple sclerosis). Denervation of the bladder was completely unsuccessful in terms of function. Incontinence and retention were both present.

Our experience to date suggests that this procedure has a place in the rehabilitation of certain patients with unsatisfactory neurogenic bladder dysfunction. Bricker's and Cordonnier's[6] experience of more than five years leads us to feel that if the ileostomy stoma is properly fashioned by excising a circular patch of skin, subcutaneous tissue and fascia, the loop will drain freely without holding urine. This is a most important technical point. If urine pools in the loop with direct ureteroileal anastomosis, reflux and pyelonephritis may be expected to occur. Perhaps a valve should be fashioned as in the performance of ureterosigmoid anastomosis.

[5] Hutch, J. A.: Vesico-ureteral reflux in the paraplegic: Cause and correction. J. Urol., **68**: 437, 1952.

[6] Cordonnier, Justin J.: Personal communication.

DEPENDENT DRAINAGE VIA THE PERINEUM IN RETROPUBIC PROSTATECTOMY

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From the Veterans Administration Hospital, Boston, Mass.

The operation of retropubic prostatectomy for benign prostatic hypertrophy has gained great popularity as it combines the complete enucleation of the obstructing tissue and the immediate excellent urinary control obtained by suprapubic prostatectomy with a minimum of postoperative hemorrhage and shock, and a much more comfortable postoperative course for the patient. However, in a small but significant percentage of cases this operation has been followed by osteitis pubis. This feared complication is serious on acccount of the prolonged incapacity and pain which it causes, and is a real potential drawback to the operation.

The prevesical space, also called the space of Retzius, or nowadays the retropubic space, becomes contaminated by urine, which is usually infected, in the course of various operations on the bladder and prostate by the abdominal route, including retropubic prostatectomy. On account of its dependent position and its tough watertight floor, formed by the endopelvic fascia and the prostatic capsule, its only avenue of drainage is upward between the undersurface of the symphysis pubis and the anterior wall of the bladder. Consequently, once it has been contaminated, its depth and its poor natural "up-hill" drainage tend to favor the pocketing of infected material and the spread of infection in the loose fatty tissue of this space. The development of such infection can be prevented by proper suprapubic drainage of this space, which is therefore considered by most operators to be essential whenever this area has been opened and contaminated.[1] Sometimes, when the drainage of this space is not adequate, infection results, and occasionally a frank abscess forms which extends by the path of least resistance upward behind the symphysis pubis to the suprapubic wound where drainage takes place.

Although opinions as to the etiology of osteitis pubis are not unanimous, the preponderance of evidence indicates that infection in the prevesical space plays an important role. Osteitis pubis was almost unknown before retropubic prostatectomy, and the great majority of cases have followed this operation.[2] In almost every case of osteitis two common denominators are present—a urinary infection exists, and the prevesical space has been opened. For practical purposes, in every instance of retropubic prostatectomy the prevesical space is exposed to possible infection through contamination with infected urine at the time of operation, and possibly later also, if leakage occurs through the suture line in the prostatic capsule. If the suprapubic drain is removed prematurely, such infection may be left undrained. It is well known that undrained urine, even

[1] Chute, R.: A note on drainage of the prevesical space. Trans. New Eng. Branch Amer. Urol. Assoc., 1938, pp. 5–8.

[2] Mortensen, H.: Osteitis pubis. J. Urol., **66:** 412–417, 1951.

when it is sterile, is irritating to the tissues.[3] Also, it has been shown that oxidized cellulose and gelatin (oxycel and gelfoam), which sometimes have been used to control oozing in the previsical space, are detrimental to wound healing, especially in the presence of infection to which they offer a favorable medium.[4] The same is true when necrotic tissue is left as a result of fulguration of bleeding vessels in or near the prostatic capsule. One or more of these circumstances just mentioned often occur following retropubic prostatectomy and favor the development of inflammation and infection which undoubtedly play a role in causing osteitis pubis. Lavalle and Hamm[5] produced important evidence in favor of an infectious etiology when they surgically biopsied the symphyses pubis of 3 patients with osteitis following retropubic prostatectomy and, using special culture methods, recovered Pseudomonas aeruginosa from all three biopsies, and in addition the Bacillus proteus in one of the cases. Microscopically the tissue showed subacute chronic inflammation involving periosteum, bone and cartilage. No suppuration was seen, but the process suggested infection of low virulence and long standing. Several nerves with advanced degenerative changes were seen. Kirz[6] also biopsied a case of osteitis following prostatectomy, and when he cut down to the bone found pus giving a scanty growth of Pseudomonas, the same organism which Lavalle and Hamm had found. On microscopic examination also much the same picture was seen, the soft tissue showing a chronic pyogenic infection, and the bone chronic inflammation. The pathologist in this case, T. C. H. Benians, said: "It is a fair assumption that the inflammation of the pubic bone and the suppuration of the adjacent soft tissues are associated processes. Both are of a mild or subacute type, the organism found, i.e., Ps. pyocyanea (pseudomonas) is not uncommonly found in old-standing infections of the bladder. . . ." The delay of several weeks before symptoms appear also suggests that a low grade infection, smouldering undrained in the loose fatty tissue of this space, very likely plays a part, perhaps by direct extension, perhaps by leading to thrombosis of the end vessels (arteries and/or veins) supplying the symphysis, which are small terminal branches from the obturator and inferior epigastric vessels. Also it is possible that interference with the nerve supply of these small vessels or to the periosteum and bone is a factor, and this could well be caused by such an infection and chronic inflammation, as was shown by Lavalle and Hamm's finding of nerves showing degeneration. No matter what the exact mechanism, infection is incriminated by the bulk of the evidence. That infection and inflammation may occur in the prevesical space without necessarily being accompanied by osteitis is evidenced by the unduly prolonged drainage from the wound which is sometimes seen following retropubic prostatectomy. Mr. Millin once told the senior author that he explained

[3] Graves, R. S. and Engel, W. J.: Experimental production of epididymitis with sterile urine; clinical implications. J. Urol., **64:** 601–613, 1950.

[4] Hinman, F. Jr. and Babcock, K. O.: Local reaction to oxidized cellulose and gelatin hemostatic agents in experimentally contaminated renal wounds. Surgery, **26:** 633–640, 1949.

[5] Lavalle, L. L. and Hamm, F. C.: Osteitis pubis: Its etiology and pathology. J. Urol., **66:** 418–423, 1951.

[6] Kirz, E.: Osteitis pubis after suprapubic operations on the bladder with a report of ten cases. Brit. J. Surg., **34:** 272–276, 1947.

the well-recognized fact that osteitis pubis is exceedingly rare following radical retropubic prostatectomy on the basis that the operative procedure removes the prostatic capsule and endopelvic fascia which form the floor of the prevesical space, and thus provides free drainage away from the symphysis. Further evidence in favor of the undrained infection theory is that osteitis pubis is unknown following either conservative or radical perineal prostatectomy, where excellent dependent drainage always exists.

In view of the evidence that infection in the prevesical space is the important factor in the etiology of osteitis pubis, which has by far its greatest incidence following retropubic prostatectomy, and of the facts that this space is exposed to contamination and possible infection in almost every such prostatectomy, and that the natural drainage of this space is poor and "uphill", with a resulting propensity to infection, it seemed to the authors that dependent drainage of the prevesical space through the perineum would be more efficient than the customary suprapubic drainage, and therefore should be better prophylaxis against the development of infection there, and thus against the occurrence of osteitis pubis. This procedure has been carried out in 8 cases in recent months with satisfactory results, and forms the basis for this report.

Drainage of the prevesical space and the region of the prostate and bladder base via the perineum is not new. One of the authors has carried this out in a number of instances following cystectomy, having had this route pointed out to him many years ago by his father, the late Dr. Arthur Chute, who used it for drainage of infection around the bladder base, and published an article on it in 1924.[7] Fullerton of Belfast, Ireland, in 1929[8] and Silverton of Sydney, Australia, in 1954,[9] both described perineal drainage of the bladder and prostatic cavity following suprapubic prostatectomy. Blockson of Oklahoma, writing in the Mexican *Revista de Urologia*,[10] advocated drainage of the prevesical space following retropubic prostatectomy by a subpubic parapenile wick as prophylaxis against osteitis—and, of course, drainage of abscess of the prostate via the perineal approach was described by the late Hugh Young many years ago.[11] The technique which the authors have used is a composite of these various earlier procedures.

Before describing the details of the technique, it seems well to mention some of the anatomical features. Figure 1 is a diagram of the pelvis in sagittal section showing the good natural dependent drainage of the prevesical space afforded by perineal drainage contrasted to the less effective "uphill" drainage by the customary suprapubic wick. In figure 2, *A*, a sketch of the male perineum, the arrow shows the path of the drainage tract. From an inch-long incision in the perineum, slightly anterior to and to the left of the anus, and not far inside the

[7] Chute, A. L.: Dependent drainage of the perivesical region. J. Urol., **11:** 365–369, 1924.
[8] Fullerton, A.: Drainage of the bladder through the perineum after suprapubic prostatectomy. Brit. J. Urol., **1:** 1–16, 1929.
[9] Silverton, R. J.: Transvesical prostatic adenomectomy with deep perineal drainage. Brit. J. Urol., **26:** 53–59, 1954.
[10] Blocksom, B. H.: Osteitis pubis. Revista de Urologia, **10:** 74–82, 1952.
[11] Young, H. H. and Davis, D. M.: Young's Practice of Urology. Philadelphia: W. B. Saunders Co., 1926, vol. 2, p. 476.

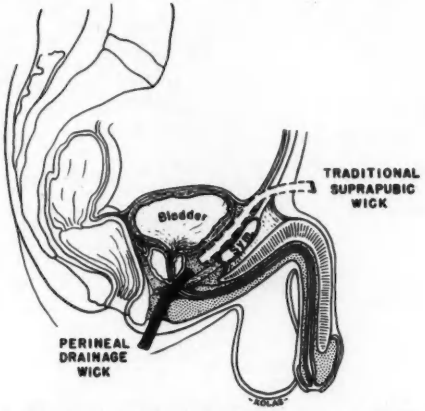

FIG. 1. Sagittal section of pelvis showing good dependent drainage of prevesical space through perineal wick contrasted with less effective "uphill" drainage from customary suprapubic wick.

pubic ramus, the dissecting finger passes just below the transversus perinei muscles (triangular ligament) and then goes upward through the left side of the upper ischiorectal fossa—superficial to the levator ani muscle—to the left side of the prostate where it pierces the endopelvic fascia, and thus enters the left side of the prevesical space through its floor. Figure 2, *B* is a diagram of a coronal section through the pelvis to include the bladder and prostate, and shows how the drainage tract goes through the left ischiorectal fossa, superficial to the levator ani muscle, and pierces the endopelvic fascia to enter the prevesical space at the left side of the prostate.

The operative technique is as follows: With the patient lying on his back, not only are the abdomen and external genitalia prepared but also the perineum, perianal region and the upper 12 inches of the inner aspect of the thighs. After the abdomen and perineum have been draped as one, assistants flex the knees and separate the thighs. A one inch vertical incision is made in the perineum slightly anterior to the anus and a little inside the left pubic ramus (fig. 3, *A*). The rather fibrous subcutaneous fat of the lower ischiorectal fossa is incised with scissors, and then the index finger of the right hand is introduced, passed easily under the lower edge of the transversus perinei muscles (triangular ligament), and then is directed upward through the upper left ischiorectal fossa in an easy plane of dissection which lies superficial to the levator ani muscle. At first the finger stays well to the lateral side of the fossa to avoid any possibility of injuring the rectum which lies in the midline. However, as the upper part of the fossa narrows, the finger comes easily and naturally to the left lateral lobe of the prostate (fig. 3, *B*). The dissection is easy, requires very little force, and is not deep or confusing. If there is any question as to the location of the prostate, this can easily be answered by passing a sound, by which the prostate can be moved somewhat and thus located. The finger is now withdrawn, and the

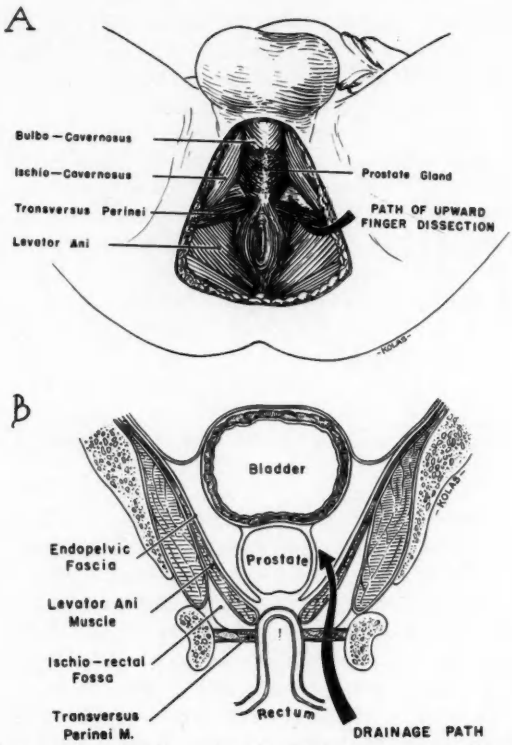

FIG. 2. *A*, diagram of perineal muscles. Arrow shows course of dissecting finger which enters perineum through small incision above and to left of anus, passes under transversus perinei muscle, then up left side of ischiorectal fossa, superficial to levator ani muscle, to left lobe of prostate. *B*, coronal section of pelvis. Arrow shows course of drainage tract which runs under transversus perinei muscle, and then up left side of ischiorectal fossa, superficial to levator ani muscle, to pierce endopelvic fascia on left side of prostate and drain prevesical space.

legs are put flat, somewhat spread apart, the whole procedure having taken but 2 or 3 minutes. Now the retropubic prostatectomy is proceeded with. After the prostate has been removed and the capsule sutured, the right forefinger is again introduced into the previously made tract in the perineum where its tip can be felt by the other hand in the abdomen just to the left of the prostate and covered by the endopelvic fascia. Although this fascia is not very thick, it is rather tough and difficult for the finger to break through. Consequently, a long, sharpish instrument, such as a dura clip applicator, is employed from above to make an opening in this fascia from the inside of the pelvis down on the finger, which is then pushed up through, thus establishing the drainage tract (fig. 3, *C*). Through this tract a soft rubber wick (Penrose) is placed to drain the prevesical space down through the perineum, where it is secured to the skin with a silk suture (fig. 3, *D*). The abdominal wound is closed without drainage. The urethral cathe-

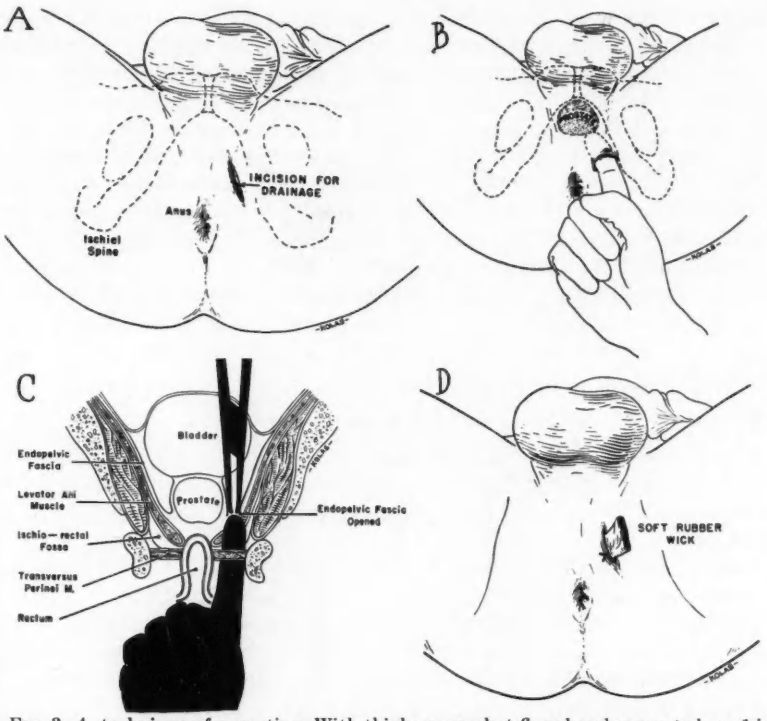

FIG. 3. *A*, technique of operation. With thighs somewhat flexed and separated, an 1 inch incision is made above and to left of anus. *B*, forefinger passes under transversus perinei muscle, and then up left side of ischiorectal fossa to left lobe of prostate. *C*, coronal section showing long pointed instrument (dura clip applicator) making opening from above in endopelvic fascia on tip of finger establishing drainage tract. *D*, perineal drain in place sutured to skin. It will not be "started" until 2 days after urethral catheter has been removed. Abdominal wound closed without drainage.

ter is left in place for one week, and the perineal drain is not "started" until 48 hours after the urethral catheter has been removed.

This technique has now been used in 8 cases in recent months with satisfactory results. The suprapubic wounds have healed cleanly and without draining. There has been no osteitis pubis, no unexplained bouts of fever, and no interference with urinary control. The only complication occurred in the second case; the senior author, when the time came to put the right forefinger back into the previously made tract and break through into the prevesical area, while feeling under the drapes inadvertently put his finger into the anus. He accomplished the break through into the prevesical space but with more difficulty than usual. The reason for this became apparent when he placed the drain, and he was horrified to find that he had drained the prevesical space into the rectum by means of a good-sized hole. For a moment ideas of such things as a proximal diverting colostomy were entertained, but then it was decided to see what

Mother Nature would do, and nothing was done other than to replace the drain in the proper perineal tract to the prevesical space and close the abdominal wound as usual, no attempt being made to repair the hole in the rectum which was hard to visualize. The urethral catheter was left in place longer than usual (2 weeks) and the drain removed 3 days later. Fortunately, no fistula of any sort occurred. However, 3 days after the removal of the drain, a small abscess pointed subcutaneously at the drain site. This was easily opened on the ward with Kelly forceps, and an ounce or so of frank pus evacuated, following which solid healing took place. The patient left the hospital in good condition and with normal voiding. He has been seen several times in the followup clinic and has continued to do nicely. Since that case the finger has always been reintroduced into the perineal drainage tract under vision. Although this mistake sounds inexcusable, it is not hard to make when working blindly under drapes, as the drainage tract and the anus are not far apart.

SUMMARY

The retropubic prostatectomy is an excellent operation for the treatment of benign prostatic hypertrophy, but osteitis pubis has followed this procedure in a small but significant percentage of cases and is a potential drawback to this operation.

There is evidence to show that infection in the prevesical space is the important factor in the etiology of osteitis pubis.

The prevesical space (space of Retzius or retropubic space) usually becomes contaminated and thus is exposed to possible infection during retropubic prostatectomy, and its poor natural drainage favors the development of infection unless it is drained properly.

The authors feel that dependent drainage of the prevesical space via the perineum must be more efficient than the usual suprapubic "uphill" drainage, and therefore should be better prophylaxis against the development of infection there, and thus against the occurrence of osteitis pubis. This procedure has been carried out in 8 cases in recent months with satisfactory results. The technique is described.

Addendum: (October 22, 1955): Since our paper was written, the procedure has been continued so that now it has been carried out in a total of 20 cases. The results have continued to be satisfactory in all cases.

A RADICAL OPERATION FOR THE CURE OF INTRACTABLE STRICTURE OF THE MALE URETHRA

ARTHUR B. CECIL

Surgeons have long hesitated to cut into the pendulous urethra for any purpose due to the great difficulty encountered in the past in closing fistulas of that portion of the urethra. Because of this, strictures of the pendulous urethra have heretofore been treated almost entirely by dilatation and by internal urethrotomy, even though these procedures offered no possibility of permanent cure.

I shall limit my discussion to an operation which I devised for the radical

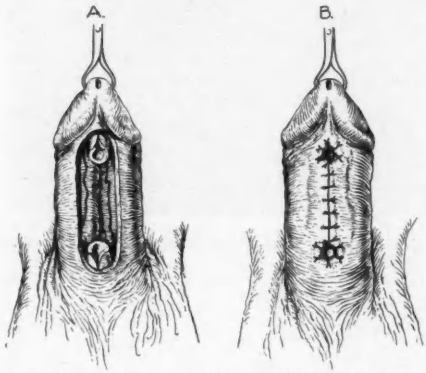

FIG. 1. *A*, strictured penile urethra has been excised. *B*, proximal and distal ends of urethra are sutured to skin edges, and skin closed along ventral surface.

cure of intractable strictures of the pendulous urethra. Johanson has recently published an article on the surgical treatment of strictures of the pendulous and deep urethra. In the treatment of strictures of the pendulous urethra Johanson divided the strictured portion of the urethra on its ventral surface, and sutured the skin to the edges of the divided strictured urethra. The urethra was later constructed by the second method of Duplay. The work of Johanson in transplanting skin of the scrotum to deeper portions of the urethra, and the excision methods as practised by Hamilton Russell and others for the cure of strictures of the deeper portions of the urethra, in my opinion will require more study. Thus, the transplantation of hair-bearing skin from the scrotum to form a part of the deep urethra will as certainly create urethral calculi as it did in the Bucknall operation.

In 1936 I described an operation for the construction of the urethra in hypospadias, and in 1946 I published an article in which I applied the technique of this operation to the cure of fistulas of the pendulous portion of the urethra, and stated that this operation would cure defects of the urethra no matter of what degree. It then occurred to me that, in intractable strictures of the pendulous

FIG. 2. Bougie has been introduced through meatus and into proximal urethra showing that urethra has been excised for 3 inches.

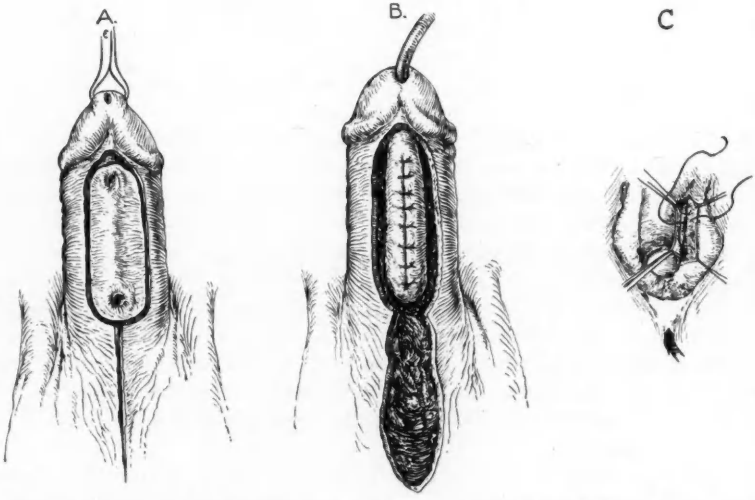

FIG. 3. *A*, incision made through skin to construct urethra over catheter; an incision has been carried down midline of scrotum for distance equal to penile incision. *B*, urethra has been constructed over catheter; tissues have been dissected back on scrotum. *C*, penis sutured down to scrotum using continuous 000 catgut suture. Skin of penis is then sutured to skin of scrotum with interrupted dermal sutures.

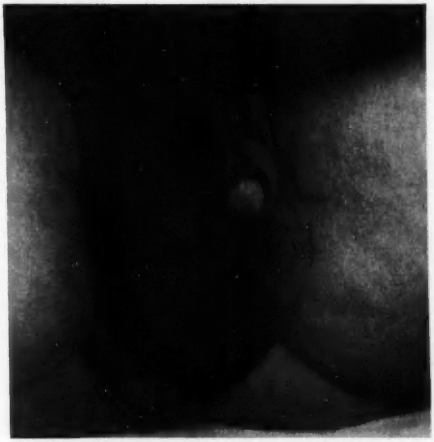

FIG. 4. Postoperative result of suturing penis to scrotum

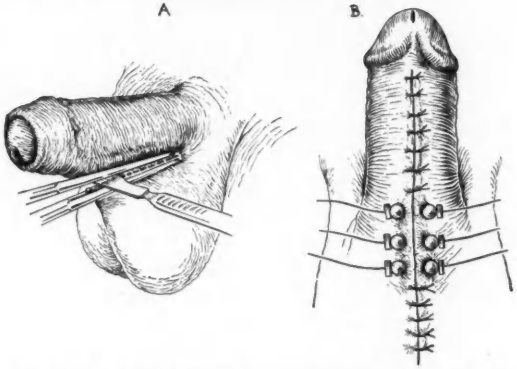

FIG. 5. *A*, two clamps are placed between scrotum and penis; penis cut free from scrotum. *B*, penile and scrotal incisions are closed. At penoscrotal angle, double lock sutures are used.

FIG. 6. Postoperative result showing cure of stricture of urethra, large size urinary stream good force. No postoperative dilatation has been necessary.

urethra, there would be no difficulty in replacing the entire portion of a strictured urethra after excising it. Accordingly, I devised the operation which I wish to demonstrate today, the steps of which are shown in figures 1 to 5. The postoperative result is shown in figure 6.

CONCLUSIONS

In the future, all strictures of the urethra that require prolonged dilatation should be treated by radical surgical methods. A study should be made as to the best method of dealing with strictures of the deeper portions of the urethra. The operation which I have described offers a perfect cure for all strictures of the pendulous urethra.

1136 W. Sixth St., Los Angeles 17, Calif.

DISCUSSION

DR. LOUIS M. ORR (Orlando, Fla.): I don't doubt that Dr. Chute probably has the answer to osteitis pubis, but I would like to ask this Association why it seems to be that osteitis pubis appears to be indigenous to certain localities.

We do a large number of retropubic prostatectomies, and it has always been our thought that osteitis pubis was due to, perhaps, infection, but also due to trauma; and when I say trauma, I mean trauma by retractors, and retractors placed on the symphysis pubis in an effort to get better exposure. I have seen some men perform retropubic prostatectomies in our localities.

We look carefully for infection prior to operation, and afterwards at the time of surgery to be certain that no retractors are placed on the pubic bone, or the symphysis pubis. The drain is pulled on about the second or third day, the catheter about the fifth or sixth day, and we have not as yet had a case of recognizable osteitis pubis.

DR. WILLIAM J. BAKER (Chicago, Ill.): I wish to direct a short discussion toward Dr. Leadbetter's presentation.

We have been interested in trying to evaluate his procedure. This slide will show the résumé of patients and the indications that we used for the procedure and the complications and results.

It is quite obvious to all of you that we have used the procedure in most instances when we could have used other methods of urinary diversion.

There are three instances on that slide where the procedure served us very well; in the second instance where we did a cystectomy, that man is in fine condition and completely rehabilitated, and then there is the lady who had obstetrical necrosis of the entire bladder base. Although young, she was an urological derelict but is now rehabilitated.

And then the last instance of a little girl 21. We have had two instances of sloughing of the stoma.

This slide shows the ureteral stomas in one of the sloughed pouches. There was certainly nothing visibly wrong with the ureteral anastomosis.

Apropos of Dr. Leadbetter's presentation, we thought the procedure was one of choice for a young lady of 21. At the age of 12, she had a spinal operation for an injured back. This left her with total urinary incontinence and partial bowel incontinence. She consulted us at the age of 18. Her mother refused consent for any operative procedures.

We placed a urethral bag catheter which she wore, changing it weekly, until she was 21 years old. We diverted her urine by means of an ileal loop on her twenty-first birthday.

This slide depicts a preoperative intravenous urogram of the young woman; certainly nothing is wrong with those kidneys.

This slide shows a three-week postoperative excretory urogram. We thought there was just slight postoperative ureteral hydronephrosis on both sides.

She resumed her work as a telephone operator one month after operation.

This slide is a picture of her ileal stoma.

This slide shows the apparatus she wears over the stoma, and this slide is a picture of her business attire.

We feel that this young woman has been rehabilitated. Her lower bowel now has a tendency toward constipation and requires daily enema, whereas before she had partial incontinence for some reason.

However, she is much more comfortable from a urinary viewpoint and quite happy with her present condition. We feel along with Dr. Leadbetter that there is a definite indication for this procedure in some of these patients. Thank you.

Dr. Edwin Davis (Omaha, Neb.): I am sure my very dear friend Richard Chute will forgive me my amazement upon reading his title. I don't believe it is necessary to explain to this audience the reason for my puzzlement.

I am reminded of a misprint on the program at the Buffalo AUA meeting several years ago, when my prostatectomy film was entitled "Perirenal Prostatectomy."

Dr. Ormond S. Culp (Rochester, Minn.): I would like to add my endorsement to two of the procedures that have been described, and also compliment all the essayists this morning.

Our experiences with the ileal pouch operation have been rather gratifying, and there are other indications which seem to justify its use. We have taken down some rather disappointing ureterosigmoidostomies and converted them to the ileal pouch with encouraging results. The pouch operation also has been successful in children, so it need not be confined to adults.

We saw one youngster with a beautiful upper urinary tract after ureterosigmoidostomy which had been performed because of exstrophy of the bladder, but unfortunately there was no anal control, so the child actually had a wet perineal colostomy. Urine was diverted to an ileal pouch, and she has been completely rehabilitated. This operation also has worked extremely well in cases of exstrophy which were seen so late that marked hydronephrosis and hydroureter precluded ureterosigmoidostomy.

Again I wish to add support to Dr. Cecil's operation. Last week I operated on my 102nd patient with hypospadias since August 1950. More than half of these cases have been completed and mostly by the Cecil operation.

Another adaptation of the Cecil operation to urethral stricture is shown in the following slides. To those of you who belong to the Correspondence Club, my humblest apologies for the repetition.

(Slide) We, too, had a patient with intractable urethral stricture. Actually, he had a congenital narrowing of his urethra from the midscrotal region to the meatus. For 20 years he had dilatations, internal urethrotomies and had worn an indwelling catheter for weeks at a time. Without exception in about two weeks he again would be urinating with difficulty and an extremely small stream. The problem was what to do with the urethra that was constricted back of the penoscrotal juncture. The terminal urethra calibrated to 12F. The proximal segment proved to have 26F caliber.

It was thought that perhaps some of the narrowed distal urethra could be used to increase the size of the constricted scrotal segment. Here is a cross-sec-

tion showing how the urethra was incised on each side as close to the corpus cavernosum as possible in the hope of preserving the remaining circumference of the urethra.

The incision on the right side of the urethra was carried to the region of the penoscrotal juncture. On the left it was carried back to the urethra of normal caliber. These incisions automatically created a flap of tissue which was turned down and interposed between the cut edges in the scrotal region. This portion of the urethra thereby was given a caliber of 22F.

An indwelling catheter was brought out at the penoscrotal juncture and later the additional urethra was constructed out to the original meatus by the two stages of Dr. Cecil's operation. No hair-bearing skin had been used in any part of the correction.

(Slide) Here is the preoperative urethrogram showing the original narrowing of the distal urethra. Here is one taken several months later showing a urethra of good caliber throughout.

Dr. Vincent O'Conor (Chicago, Ill.): I would like to digress a little and ask this group just what is meant by osteitis pubis.

I don't think anybody has ever been able to correlate the initial incidence of osteitis pubis with cultural infection, and I would like to recite an experience which might be interesting and instructive.

We have had on our service 4 cases of osteitis pubis in the last 12 years, all of which have followed transurethral resection of the prostate. One of these patients was a personal friend of mine; I cut too deeply into the area and I had to drain him retropubically shortly after I finished the resection. This man finally got well after 6 or 7 months, but during that six or seven months he was in a great deal of agony.

In discussing the subject of osteitis pubis with one of our orthopedic men, whom I consider something of a genius and a man of great talent, he said, "You urologists are crazy. You don't understand the mechanism of osteitis pubis at all. It is not primarily an infectious disease at all; rather, it is due to a foreign body.

"What happens is that circulation of the pubic ramus is interfered with. A sloughing of the cartilaginous tissue, which unites the symphysis, results. The aftermath is a foreign body, and until that foreign body is absorbed, the patient has an irritative lesion and he won't get well."

I did not agree with that. But it so happened that during the last 3 years we operated upon a couple of patients who were referred to us by him, and as things would happen, osteitis pubis developed in both of these men. Of course, both of these patients came back to the orthopedic surgeon and not to me.

I saw these two patients. I saw the operation on their pubes. I saw him remove the triangular chunk of necrotic tissue from the symphysis, and I saw those patients walk out of the hospital completely relieved of symptoms and cured in less than a week.

Dr. Frank C. Hamm (Brooklyn, N. Y.): The evidence that osteitis pubis is an inflammatory process is so overwhelming that it is difficult to understand anyone denying it. All the familiar clinical signs of infection were observed in

our cases; low grade fever and leukocytosis were constant findings. And in 3 patients in whom a biopsy of the symphysis was done during the acute phase, necrotic purulent tissue was found. When subjected to culture Pseudomonas aeruginosa was recovered in all three; in one instance it was combined with Proteus.

The Pseudomonas is normally of low virulence, but some members of this large family of organisms are not all completely harmless. The ophthalmologist tells us that some of the more resistant types of corneal ulcer result from Pseudomonas. The otolaryngologists make essentially the same observation about middle ear infections. Microscopic examination of the removed tissue confirmed the opinion that it is a true osteomyelitis.

I doubt that retropubic prostatectomy had much to do with the wave of osteitis pubis that appeared simultaneously with the introduction of this operation. The wide usage of chemotherapy and antibiotics appeared at the same time. It is well known that none of these agents is effective against Pseudomonas—in fact, evidence at hand indicates that the opposite is probably true, that the pathogenicity is actually increased.

Dr. John R. Hand (Portland, Ore.): I agree with Dr. Chute that osteitis pubis is a dread disease, and that every means should be taken to prevent it. However, we have done some 275 retropubic prostatectomies without osteitis pubis. I would hate to think that this was just good luck. I believe the following points in technique are important in its avoidance.

Like Dr. Orr, we do not use retractors anteriorly. We make the midline incision, separate the recti, then insert lateral retractors. After this we continue the incision right down to the pubis so that as further lateral retraction is made there will be less tension on the rectus fascia at its insertion into the pubis.

After the prostatic capsule and bladder have been incised the first thing we do is to irrigate the space of Retzius with saline solution. We then proceed with the retropubic prostatectomy. After the bladder and prostatic capsule have been closed with one layer of interrupted plain sutures, we again wash out the space of Retzius.

Dr. Samuel A. Vest (Charlottesville, Va.): I would like to make one comment on Dr. Creevy's paper, and call attention to electromyography in this condition.

Dr. William J. Engel of the Cleveland Clinic referred to us a young woman who had been catheterizing herself for 7 years. She had a large atonic bladder, and we carried out the diagnostic procedure of determining her electromotive force and pattern with an instrument that we reported several years ago.

Much to our surprise, this girl could not void but she had normal voltage in the bladder. She had a normal pattern of waves and a normal frequency, which indicated that she had normal autonomic nerves, and normal bombardment of her muscular system. The muscle of the bladder, however, had secondarily atrophied.

We were perplexed about this, and we studied her very carefully; neurologic examination by a fine neurologist was negative, also by the gynecologist. The only other thing is that she had no sensation during intercourse, but normal sensation in the vagina.

At a meeting of the Virginia State Medical Society I met a physician from the patient's home town, about 400 miles from our place. I asked him about her, and he said, "Well, I've known her all her life. She is my next door neighbor. She went to college and took a course in physiology, and she brought up questions of pregnancy. She had a nervous breakdown and had to go into an institution. No one knew that. She began to have mental difficulty at that time. Her husband didn't even know it."

Going back to the history, he told me that, right after she was married, she suddenly began to palpate a mass herself above the symphysis, that by catheterization he determined that the mass was her bladder. To make a long story short, we suspected and diagnosed by a method of electromyography that this was a functional matter with her, which she had subconsciously or consciously connected with pregnancy, sex, marriage, reproduction, etc., retained her urine until she finally had achieved muscle atony, but with unquestionably a normal autonomic system.

I recommended partial resection of the bladder, which the patient refused, and said she would much rather prefer going on catheterizing herself.

One other comment about the drainage in retropubic prostatectomy. In the first 25 cases of retropubic operations that we did in our clinic, we encountered 4 cases of osteitis pubis, and I believe we made the first report in this country of osteitis pubis as a complication of retropubic prostatectomy.

After that we did 200 cases without any further osteitis. I don't know how many cases of retropubic prostatectomy that we have done during the last three or four years, but we have had no further examples of osteitis.

I don't know why osteitis pubis occurred in our first 25 cases. Maybe we have refined our technique. Maybe now we have used more or less routinely different antibiotics, but I get the general impression in talking to urologists in my area and over the country, that this first wave of osteitis, whatever the cause of it, has more or less subsided, and it does not seem to be the problem that it was several years ago.

We would have had to do about 200 cases by Dr. Chute's method, without osteitis, and even then we could not state that its absence was due to the use of his perineal drain.

Dr. Wyland F. Leadbetter (Boston, Mass.): (Closing) I wish to thank Drs. Baker and Culp for their discussion. I don't know how many of you have had experience with the ileal loop. It occurs to me that there are one or two points of technique which are important, and one which might explain Dr. Baker's trouble with that particular loop.

Since this is a free draining loop and not intended to hold any urine, it is most important that the opening through the abdominal wall be made large, and the best way to do it is to actually cut out a circular area of fascia, skin and subcutaneous tissue, so that the fascia cannot come together and squeeze the loop of bowel.

If this isn't done, there is a tendency for loops to decompensate and hold urine, which defeats its purpose. Also it may interfere with blood supply to the

terminal portion of the loop. I think this is one of the most important points, aside from utilizing a portion of bowel which is well vascularized.

DR. RICHARD CHUTE (Boston, Mass.): (Closing) I am delighted that my small presentation has evoked so much interest, but I don't think I can answer all the questions.

I do agree with Dr. Hamm that, although trauma, as suggested by Louis Orr, and various imponderables probably may play a part, practically always, you do have the facts that the prevesical space has been opened, and you have had potential infection there. I feel that very strongly.

I agree especially with Dr. Henry Weyrauch that it is really dangerous to suture the capsule and then take out your drain in a couple of days, because if you have the leakage through the capsule, as you may well have if you remove the catheter within a week, the material which leaked is imprisoned there. I feel very strongly about this and agree with Dr. Weyrauch that it is important to leave the wick in place, either above or below, until after the catheter has been out for 24 hours.

What I like about perineal drainage is that it is so natural. It is not uphill, and honestly the whole thing doesn't add five minutes to the operation.

I want to thank all my discussors. I also think that Dr. O'Conor's idea of the foreign body is a stimulating one.

CARCINOMA OF THE MALE AND FEMALE URETHRA: PATHOLOGY AND DIAGNOSIS

ARCHIE L. DEAN

CARCINOMA OF THE MALE URETHRA

Pathology. The epithelium lining the male urethra is composed of many layers of cells. Proximally it closely resembles the transitional epithelium of the bladder with which it is continuous at the internal urethral orifice. Throughout the cavernous portion of the canal, the lining cells are columnar while distally, in the fossa navicularis, they become flat. Although the great majority of urethral cancers in men arise from columnar epithelium in the cavernous urethra, with few exceptions, the neoplasms are composed of squamous cells. This is probably the result of chronic irritation bringing about squamous metaplasia and malignant degeneration.

Urethral tumors are commonly classified according to their place of origin but since the anatomical divisions of cavernous, membranous and prostatic urethra are inconsistent with clinical experience, the presently accepted clinical divisions of the urethra for tumor location are penile, bulbomembranous and prostatic, respectively. Primary tumors of the prostatic urethra are exceedingly rare. A majority of the growths develop in the bulbomembranous urethra and involve the perineum. Since approximately 20 per cent of the tumors of the penile urethra arise in the fossa navicularis from external virus infections or as the result of congenital meatal strictures and since these growths can be treated more conservatively and have a definitely better prognosis, the clinical problem is simplified by classifying them separately.

Etiology. Between 1926 and 1954, 59 patients with urethral cancers were examined and treated at the Memorial Hospital. Of these patients, 46 were women and 13 were men, a ratio of nearly 4 to 1. The average age of men when the urethral cancer is discovered is said to be about 55 years and the age of greatest incidence about 60 years. The average age of the Memorial Hospital patients at admission was 64 years. While predominantly a disease of the elderly, it has been reported in a youth of 18 years.

The great majority of urethral cancers arise apparently from the effects of chronic irritation. In rare instances no contributing cause can be found. About 75 per cent of the patients suffered from chronic urethral irritation produced by recognized strictures, infections or trauma. The frequent association of urethral strictures and subsequent cancers at the stricture site has long been recognized. While the majority of observers have found about 50 per cent of urethral cancers superimposed on strictures, an incidence as high as 76 per cent has been reported. Strictures from straddle injuries are followed by urethral cancers with especial frequency, possibly because they are composed of so much contracting scar tissue that they produce tight stenoses and perhaps because the mucosa of the bulbomembranous urethra when chronically irritated more readily undergoes malignant degeneration.

Gonococcal infections, which in the past gave rise to a large proportion of precancerous strictures, seldom have been described as so closely preceding discovery of a tumor as to be a precipitating cause. On the other hand, mixed infections, largely maintained by strictures, probably play a considerable part in producing long-standing urethral irritation. Their frequency and virulence are demonstrated by the common occurrence of periurethral abscesses as stricture complications.

The trauma usually mentioned in the etiology of urethral cancers is produced by the passage of sounds. I doubt its importance. At any rate, when sounds are necessary, most, if not all, of the other causative agents have been present for some time. However, there is often a close time relationship between the use of sounds and discovery of a tumor.

The most common tumor of the penile urethra is the delicate papilloma which usually arises from the distal 2 cm. of the fossa navicularis. These benign growths are said to result from virus infections. In a number of tumors of the urethral meatus, with no other influence apparent, it has appeared reasonable to ascribe considerable etiological importance to the repeated trauma of the urinary stream impinging on the mucosal rim of the stenosed meatus. The effects of such irritation in the penile or bulbomembranous urethras have not been recognized.

Except for the unusual direct extension of a bladder tumor along transitional epithelium to the posterior urethra, no urethral cancers have been described as possibly resulting from the chronic irritation of cancerigenic substances in the urine. This is noteworthy since tumors of the ureter and the bladder follow tumors of the kidney pelvis so regularly as to be expected. The rarity of urethral cancers in patients with pre-existing tumors of transitional epithelium suggests that the mucosa of the urethra may be more resistant to chronic irritation from cancerigens in the urine or that the urine remains in contact with urethral mucosa for too short a time to initiate changes. However, the fact that tumors in an otherwise normal urethra may occur in patients with no evidence of disease in the upper urinary tract could be interpreted as evidence that urethral mucosa may be extraordinarily sensitive to irritants in the urine. Possibly the rapid and forceful passage of urine containing crystals may subject the normal urethra to a form of irritation absent in the upper urinary tract. Such possibly far fetched speculation appears permissible because it is likely that all of the influences producing urethral cancers are, as yet, unknown.

After years of chronic urethral irritation, usually from obvious causes but occasionally without any preceding disease, the cancer begins to grow. It expands and infiltrates, destroying the urethra in its progress and invading the periurethral tissues and the corpora cavernosa.

The literature repeatedly contains the statement that urethral cancers remain localized for a long time. It is true that as a group squamous cancers do not metastasize as early in their development as certain other tumors but the length of time a specific neoplasm remains localized is difficult to measure because one rarely knows just when malignancy first appears. This information in the urethra is seldom apparent. The clinician soon learns to place no dependence on a urethral

tumor to remain localized after experience shows the frequent presence of metastases when the tumor is first recognized.

The male urethra is richly supplied with lymphatics. Those from the penile urethra drain into deep subinguinal nodes which communicate with external iliac nodes. Lymphatics from the bulbomembranous urethra communicate with external iliac and pubogluteal nodes, while those of the prostatic urethra unite with the other lymph vessels of the prostate and drain into a cephalad group of external iliac nodes. It is evident, therefore, that lymph-borne metastases from urethral tumors are likely to be inaccessible to clinical investigation unless exposed surgically. After tumors grow from the urethra into the cavernous tissues, widespread dissemination through the bloodstream may occur.

Symptoms. There are no precancerous symptoms or characteristic early symptoms of urethral cancers in men. For a considerable time the clinical picture is that of stricture. When the tumor produces symptoms, it is well advanced. Pain during erections is one of the earliest symptoms and a sticking, burning pain during urination soon ensues. Following ulceration of the growth, a serosanguinous urethral discharge having the offensive odor of necrosis is likely to develop.

A cancer must be suspected when the patient reports that his accustomed treatment with sounds was followed by unusually active bleeding which continued for a longer time or that his stricture closed unusually soon following dilatation. Not infrequently, closure of the urethra is complete. Sometimes spontaneously, more often after the passage of sounds, a painful, inflamed, indurated area may appear in the periurethral tissues external to the stricture. If this is incised to drain a periurethral abscess, grumous material rather than pus may be evacuated and a rapidly growing, fungating tumor develops around a fistula. Before this event, or soon afterward, if the growth is in the penile urethra, subinguinal nodes may become palpable.

When a urethral tumor is not preceded by a stricture, the earliest symptom may be a spontaneous blood-tinged urethral discharge. After such a growth becomes obstructive, dilatation is likely to cause unusually active bleeding because the constriction is produced entirely by delicate and highly vascular tissue.

Tumors which arise in the fossa navicularis are usually discovered by the patient himself. He is often led to examine the canal by observing that his urinary stream has become slower or that it has assumed an unusual shape. Tumors which arise at the edges of the meatus appear at first as insignificantly small sores. They grow slowly but steadily in spite of treatment with home remedies.

See figures 1 to 4.

Diagnosis. In the writer's experience, the diagnosis of urethral tumors in men is usually easy because, with few exceptions, at the time of examination the disease is far advanced. Such self-evident diagnoses, however, are of little more than academic interest because, with the exception of tumors of the meatus and fossa navicularis, practically all of these patients are incurable. On the other hand, the discovery of urethral cancers sufficiently early for treatment with a fair chance of a cure is exceedingly difficult and it seldom has been accomplished.

Each patient with urethral obstruction must be examined with lively aware-

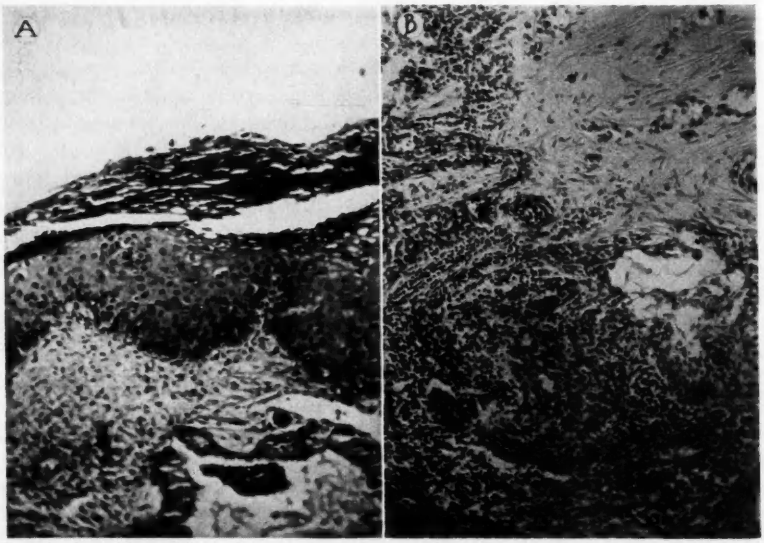

FIG. 1. *A*, epidermoid carcinoma of urethra, grade 3. *B*, metastasis in lymph node from primary tumor shown in *A*.

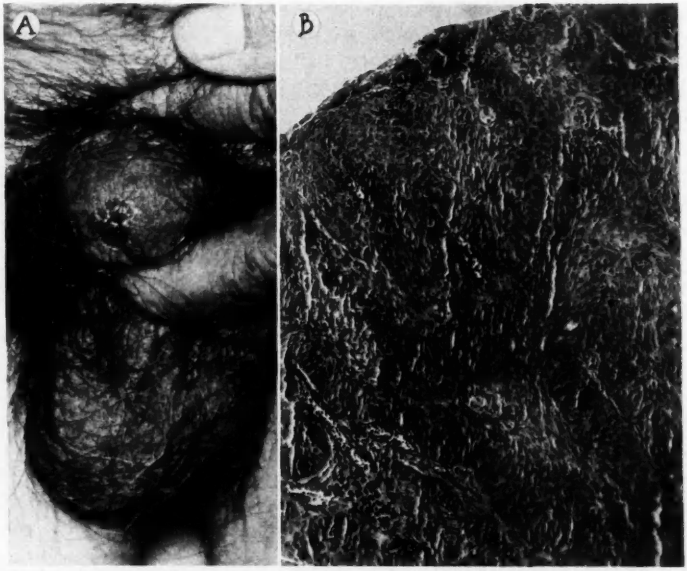

FIG. 2. *A*, primary carcinoma at urethral meatus. Patient observed this small sore growing gradually for 6 months. *B*, innocent appearing lesion shown in *A* proved to be squamous carcinoma, grade 3, as shown in figure 1, *A*.

ness that he may have a cancer. This is essential not only because early recognition of the tumor requires that special tests be performed but also because one must avoid certain common measures which could aggravate the disease.

The diagnosis of a urethral cancer must be established by microscopic examination of material from the growth. Biopsies from fungating periurethral lesions need not be discussed but in order to prevent such disasters, investigation of periurethral induration must be made from within the canal. I know of no successes with cytological examinations and doubt whether urethral tumors are generally suitable for such investigations. Since most tumors begin to grow proximal to strictures, the endoscope seldom approaches them close enough to provide a clear view. For the same reason, urethrograms are usually unsatisfactory and, for the most part, show only the stricture. On the other hand, tumors growing independently of strictures can be visualized and adequate specimens can be removed from them with a cystoscopic rongeur. No instrument has been devised especially for performing biopsies on urethral tumors but the writer has found a ring curette of approximately 3 mm. diameter quite satisfactory for reaching the tumors and obtaining scrapings which may be embedded in paraffin and sectioned. About 90 per cent of the tumors prove to be squamous cancers while 10 per cent are papillary or transitional cell tumors or adenocarcinomas. Two women in the Memorial Hospital group had primary melanomas of the urethra but similar growths were not found in men.

The presence of metastases also should be established by microscopic examinations whenever possible. If the tumor originates in the penile urethra, failure to detect adenopathy in subinguinal nodes or failure to find microscopic evidence of cancer in enlarged nodes is good evidence but not positive proof that the disease is localized. Cancers in the bulbomembranous and prostatic urethras probably have metastasized by the time of their discovery, whether or not such extensions can be found. Excretory urograms may show pressure on the bladder or displacement of the lower ureter but only if metastatic pelvic nodes have become greatly enlarged. Careful surgical scrutiny of the external and internal iliac

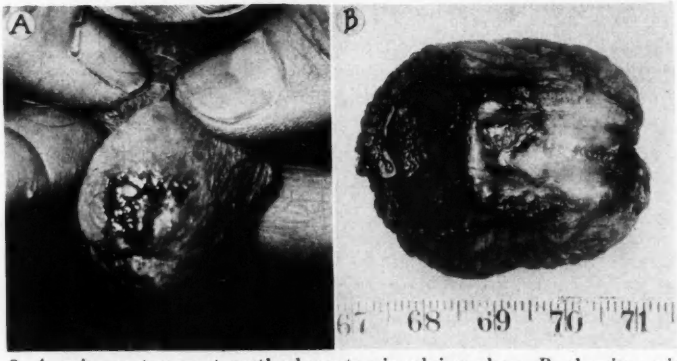

FIG. 3. *A*, primary tumor at urethral meatus involving glans. *B*, showing origin near meatus of tumor depicted in *A*.

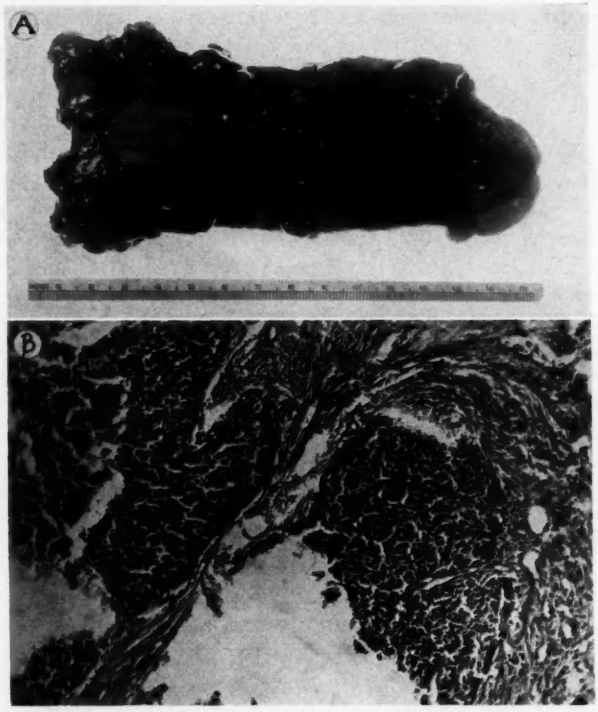

FIG. 4. *A*, carcinoma of penile urethra with no preceding stricture or other recognizable source of chronic irritation. *B*, photomicrograph of gross specimen shown in *A*.

lymphatics probably is the most accurate way to show extensions of the disease through lymphatics but here, as with bladder tumors, there is likely to be at least a 10 per cent factor of error due to metastases which are inaccessible or occult. Finally, roentgenograms of the chest should be made in a search of blood-borne metastases.

If superficial tumors of a low grade of malignancy have spread from the bladder to the prostatic urethra, it is probable that, when found, the disease is confined to these organs. Infiltrating bladder tumors spread to the prostatic urethra much less frequently but at the time of their discovery, metastasis is likely.

CARCINOMA OF THE FEMALE URETHRA

The female urethra is a canal 2.5 to 4.0 cm. in length. It represents only the proximal portion of the male urethra. The posterior wall, except in its most proximal portion, is intimately connected with the anterior wall of the vagina. The external orifice lies between the labia minora. Local expansion and infiltration of a urethral cancer, therefore, invade these structures early with produc-

tion of the usual vulvourethral tumor. The epithelium lining the canal, in its proximal portion, is transitional in type, continuous with that of the bladder; distally it becomes squamous. This junction of columnar and stratified squamous epithelium, like that of the lip and anus, constitutes an area peculiarly subject to malignant degeneration. The submucosa of the wall of the urethra is highly vascular. It is also richly supplied with lymphatics. These have terminations similar to those of the membranous and prostatic portions of the male urethra, passing to relatively inaccessible hypogastric nodes, to the medial suprafemoral nodes of the external iliac group and to the uppermost nodes of the external iliac group. The lymph vessels of the urethrovaginal region and labia minora anastomose and pass to the superficial subinguinal nodes. Involvement of these readily palpable nodes in the female, therefore, is evidence of considerable local tumor spread and probable involvement of nodes in the pelvis, whereas in carcinoma of the penile urethra, it usually indicates the earliest metastasis.

See figure 5.

Etiology. The average age of women at the time of discovery of a urethral tumor is said to be about 52 years; in the Memorial Hospital group it was 57. While there may be great differences in age between the youngest and the oldest patients (in this series they were 35 and 75 years, respectively), the majority of the women were well beyond the menopause. Practically all were or had been married; the great majority, but not all, had had children. The past histories of women with urethral cancers showed no unusual features nor, previous to the onset of symptoms, were there significant references to the genitourinary tract.

As in men, urethral cancers in women have been attributed to chronic irritation and there is no reason to minimize the importance of this agent. However, in women, it is likely to be more difficult to recognize the causes of chronic irritation which in a given patient produces a urethral cancer. Possible causes are numerous, such as gonococcal and luetic infections and lymphogranuloma venereum.

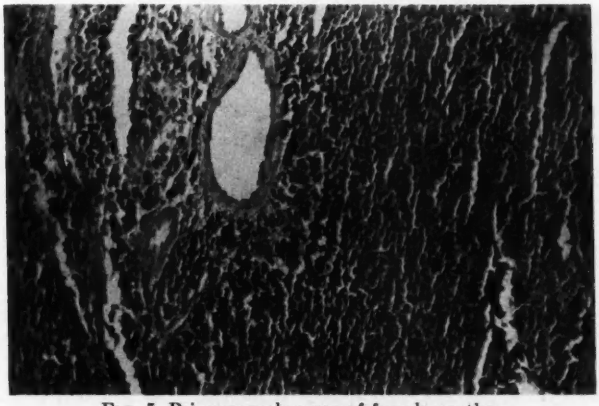

FIG. 5. Primary melanoma of female urethra

Each of these may induce stenosis of the canal which further augments irritation. Mixed infections in congenital or acquired diverticula also are potent sources of both subacute and chronic urethritis. Birth injuries may leave changes such as strictures or eversion of the urethral mucosa which are recognized sources of chronic irritation and have been known to precede cancers. Bladder tumors in women seldom extend spontaneously into the urethra. Furthermore, urethral tumors in women rarely have been observed in individuals who have had tumors of transitional epithelium in the kidney, the ureter, or the bladder which could be attributed to the chronic irritation of cancerigens in the urine.

After a period of years during which the urethra has been subjected to the various types of irritation mentioned and perhaps also to other influences as yet unrecognized, a cancer or some other manifestation of chronic irritation may appear. The most common of the noncancerous changes are granular urethritis and productive lesions such as caruncles, papillomas and polyps. Recognition of any of these conditions calls for their prompt eradication and correction of the condition which produced them because their presence indicates that the factors which may produce a cancer have been in operation for some time.

In studying the etiology of urethral cancers in women, one is struck by the frequency of definite manifestations of chronic urethral irritation and the scarcity of urethral cancers and by the number of established urethral cancers in patients who described no previous urethral complaints.

Symptoms. Women may experience many symptoms from urethral cancers but hardly any occur before the growth is well established. There may be frequency, nocturia, urgency and intermittent, burning, terminal dysuria. Later there is likely to be dyspareunia, intermittent blood-tinged discharge, a slowing of the urinary stream, gradually increasing incontinence and finally greatly increased urinary difficulties, pain in the lower abdomen and complete retention. When the sequence of symptoms was clear, complete retention occurred about six months after the onset of frequency and nocturia. While individuals may seek relief from any of these symptoms, an unfortunately large proportion of patients were first examined when in complete retention. An occasional patient visited a physician after discovering a mass in the vulva and others some time after finding enlarging inguinal nodes.

Diagnosis. When discovered, urethral cancers in women usually appear as dark red productive lesions growing from the urethral meatus. There may be an exuberance of tissue to form a rosette 1 cm. or more in width. On the other hand, the meatus may be only slightly pink and swollen or a growth may protrude from within the canal while its rim is apparently uninvolved. The labia minora may appear distorted by contractures without abnormal changes in color or they may be destroyed by the spreading ulcer. Palpation shows more accurately the nature of the disease and its extent. The urethra usually is densely indurated and the common vulvourethral involvement can be felt radiating from the urethra for varying distances. Vaginal examinations usually are painful and the orifice may be stenosed. A relaxing anesthesia, therefore, and a rectal approach may be necessary when examining the pelvis for enlarged nodes. Subinguinal lymph

nodes usually are enlarged; to determine whether or not they are cancerous requires special investigation.

Endoscopic examinations are feasible with cancers of the female urethra although a traumatizing preliminary dilatation often is necessary. An ulcerating growth usually is seen and perhaps palpation against the instrument may outline the lesion more clearly. The most encouraging picture shows the growth limited to the distal urethra and thus possibly amenable to successful treatment. It is interesting to note that hypertrophy of the bladder musculature sufficient to produce trabeculation has been a common finding. Excretion urograms frequently show ureteral obstruction.

The diagnosis of cancer of the female urethra must always be established by the microscopic examination of adequate tissue from the lesion. As in the male, the great majority prove to be squamous cancers. Tumors of grades 2 and 3 predominate and different grades of malignancy may be represented in different portions of the same growth. A small proportion are papillary tumors, adenocarcinomas, polypoid tumors or mucoid tumors. Two patients in the Memorial Hospital series had primary melanomas. The true nature of inguinal adenopathy also should be proved histologically although extensive metastatic disease may exist deep in the pelvis without demonstrable involvement in the groins.

Among other important reasons for accepting only the positive biopsy as evidence of a urethral cancer is the difficulty of differentiating the neoplasm from productive lesions by clinical means. This is especially true of the urethral caruncle which is a benign vascular tumor which usually grows from the posterior wall of the urethra near the meatus. Caruncles may produce a burning pain, painful urination and bleeding. Caruncles do not invade the vulva nor do they infiltrate the wall of the urethra. Nevertheless, without a biopsy caruncles may be mistaken for cancers, cancers may be mistaken for caruncles, or cancers and caruncles may coexist with the malignant lesion masked by the benign.

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THE TREATMENT OF URETHRAL TUMORS

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The treatment of urethral tumors will vary according to the sex of the patient, the location of the tumor, the local extent of the tumor, histological type of the tumor, and the presence or absence of metastases which may travel not only along the lymphatics, but also along the blood channels (fig. 1). Since primary cancer of the urethra, in both the male and female, is rare, and presents many variations, both in histology, location, and extent, generalizations with regard to therapy are difficult and individualization of therapy is necessary (table 1).

A study of the majority of the reported cases of male urethral tumors indicates that the armamentarium used for therapy has been 1) surgical excision or destruction of the tumor; 2) local application of some form of irradiation; 3) treatment of the lymph nodes; 4) palliative therapy. It has also very definitely shown that the problems posed and the results obtained are definitely related to the location of the tumor. Tumors arising in that portion of the urethra distal to the bulbous portion have apparently been recognized earlier, have posed less problems of therapy and yielded significantly better results than those arising in the bulbous, membranous or prostatic urethras (table 2).

From a review of the reported cases it would seem that about a third of the carcinomas of the urethra arise in that portion of the urethra which is distal to the bulbous portion. Surgical removal or destruction is the treatment of choice when the tumor is present in this locale. Of the 65 collected cases reported by Kreutzmann and Colloff,[1] 35 were cured. The type of therapy in these 35 is outlined in table 3. It will be noted that surgical removal of the involved area either alone or in conjunction with irradiation and removal of the regional lymph nodes was carried out in 33 of the 35. Radiation alone was used in 2 of the 35. In 9 instances the regional lymph nodes were removed in addition to local removal of the tumor. In one instance radiation of the regional lymph nodes was carried out, and in two instances local radiation plus surgical excision was carried out locally. Emasculation has been described as part of the surgical therapy in tumor of the anterior urethra. It is rarely indicated except with extensive local involvement of the skin and scrotum, and the probabilities are that when this is necessary, the tumor is inoperable. In Hotchkiss'[2] report of 5 cases involving this portion of the urethra, the results of local surgical removal were poor. It is probable because of his report of the high incidence of lymph node involvement that surgical therapy was applied relatively late in the course of the disease.

Only 2 cases of tumor involving the penile urethra were seen in the University Hospitals in the 20-year period between 1935 and 1955. Both of these presented papillary tumors which responded well to destruction by coagulation. No other

[1] Kreutzmann, H. A. R. and Colloff, B.: Primary carcinoma of the male urethra. Arch. Surg., **39:** 513–529, 1939.

[2] Hotchkiss, R. S. and Amelar, R. A.: Primary carcinoma of the male urethra. J. Urol., **72:** 1181, 1954.

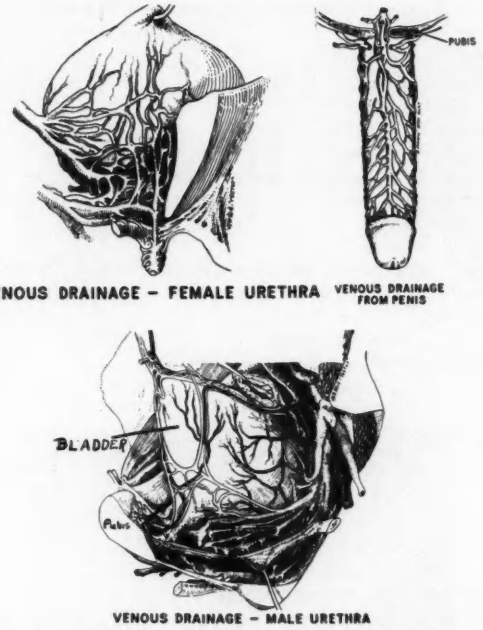

FIG. 1. Note profuse venous drainage from urethra in both sexes

TABLE 1. *Tumors of the urethra: Factors influencing therapy*

I.	Local extent.—Breakdown of continuity of urethra especially as evidenced by abscess formation; infection; local rapid extension in new fascial plane.
II.	Histological malignancy
III.	Location
	a) Penile urethra
	b) Bulbous urethra
	c) Membranous and prostatic urethra
IV.	Metastasis
	a) Lymphogenous
	b) Hematogenous
V.	Other findings
	Due to local disease
	Due to general disease

treatment was carried out and the results were good, cures being obtained. See figure 2.

It would seem therefore that the basic therapy of tumors involving the penile urethra is surgical destruction. In most instances, because of a possibility of invasion of the corpora cavernosa, partial or radical penile amputation with the construction of a perineal urethrostomy is indicated. Local irradiation has rarely

TABLE 2. *Treatment of carcinoma of the urethra*

1. Surgical removal
2. Coagulation after exposure
3. Management of the lymphatics
   a) Embolic phenomenon (Willis)
   b) Anatomical considerations
      1) The network continuous with prostate and bladder
      b) The presymphyseal nodes
      3) The inguinal nodes
      4) The pelvic nodes
   c) Retrograde and irregular spread—possibility of blockage by infection reaction
   d) Surgical removal
   e) Radiation therapy
4. Local destruction by radiation therapy
   Radium needles, radon seeds, radium pack, isotopes
5. Palliative

TABLE 3. *Tumors of the penile urethra (collected series, Kreutzmann and Colloff 1939)*

Total 65; recovered, 35

Treatment in the 35 that recovered:	
Radical amputation + adenectomy	8
Extirpation of urethra + adenectomy	1
Amputation alone	20
Extirpation of urethra alone	1
Radiation alone	2
Amputation + radiation	2
Extirpation of urethra + x-ray to glands	1

FIG. 2. Case of papillary tumor of penile urethra successfully treated by destruction with coagulating current.

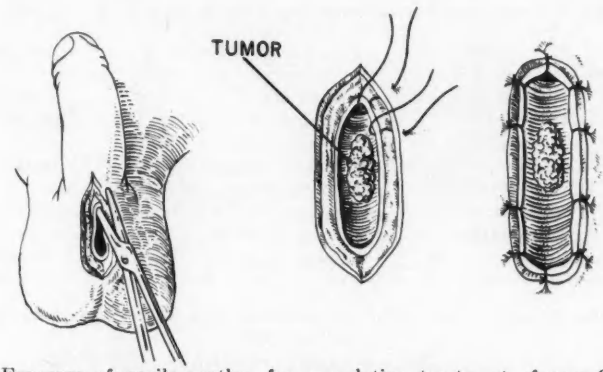

FIG. 3. Exposure of penile urethra for coagulation treatment of superficial tumor. Closure after several months of observation may be carried out by Johanson technique.

FIG. 4. Note bridge of skin which can be utilized to construct new urethra. Young's technique effects direct anastomosis between membranous and penile urethra.

been used and upon logical grounds is not as sure of destroying the lesion as surgery or cautery. The latter can be performed extensively through a temporary urethrostomy with later reconstruction of the urethra by a modification of the technique of Johanson[3] for extensive stricture of the urethra (fig. 3).

Tumors involving the bulbous, membranous and prostatic portion of the urethra make up at least two thirds of the primary cancers of the male urethra. A small portion of these, however, do not extend posteriorly to any great extent and involve mostly the more distal portion of the bulbous urethra. These may be considered separately and are almost as accessible to surgical therapy as the tumors in the more distal portion of the urethra. The operation described by

[3] Johanson, B.: Reconstruction of the male urethra in strictures. Acta Chir. Scandinav., Supp. 176, 1953.

TABLE 4. *Carcinoma of male urethra: University of Iowa Hospitals, 1935–1955*

No.	Case	Location	Treatment	Result
1	J. G.	Anterior	Coagulation	"Cured"
2	K. J.	Anterior	Coagulation	"Cured"
3	M. C.	Prostatic	Coagulation	Death
4	S. H.	Bulbous perineal extravasation	3000 R-irradiation S.P. cystostomy	Death
5	J. P.	Bulbous perineal extravasation	Radical with colostomy; nodes not involved	Died postoperatively
6	W. W.	Bulbous	Local excision	"Cured"

TABLE 5. *Tumors of bulbous, membranous, and prostatic urethra (collected series, Kreutzmann and Colloff 1939)*

Total, 77 cases; 9 recovered

Treatment in the 9 that recovered:	
Emasculation + adenectomy	1
Amputation + adenectomy	1
Amputation + adenectomy + x-ray	1
Excision of urethra + adenectomy	1
Amputation—radical	1
Resection of urethra + cystostomy	1
Amputation of penis + cystostomy	1
Resection of urethra + x-ray to glands	1
Excision of growth + local radium	1

Young[4] consisting essentially of a dissection of the bulbous urethra and the adjacent corpora with anastomosis of the distal anterior urethra to the membranous urethra is an example of the type of operative procedure which can be carried out in the smaller lesions located in this area. Essentially the same type of operative procedure was performed in the one case involving the distal portion of the bulbous urethra which occurred in our series (fig. 4). In this case resection of the urethra was accomplished leaving a perineal urethrostomy and a bridge of skin which could be used later for reconstruction of the urethra should the patient so desire (table 4).

When the more proximal portion of the bulbous urethra is involved or the membranous portion is involved, much more radical local procedure is necessary if a satisfactory excision of the local lesion is to be accomplished (table 5). Lesions involving the membranous urethra almost invariably extend through the urethral wall and will necessitate extensive removal of the bulbous urethra, the entire membranous urethra and the surrounding structures involving the superficial and deep layers of the triangular ligament and the structures between them. An operative procedure such as described by Uhle[5] or Goodwin[6] is indi-

[4] Young, H. H.: A new radical operation for carcinoma of the bulbous urethra. Surg., Gynec. & Obst., **68:** 77–86, 1939.

[5] Uhle, C. W. and Holfelner, E. D.: Treatment of carcinoma of male urethra by radical surgical infrapubic removal. J. Urol., **68:** 302, 1952.

[6] Kaufman, J. J. and Goodwin, W. E.: Carcinoma of the male urethra: One stage surgical treatment by radical perineal excision and rectal transplantation of the divided trigone. Surg., Gynec. & Obst., **97:** 627–632, 1953.

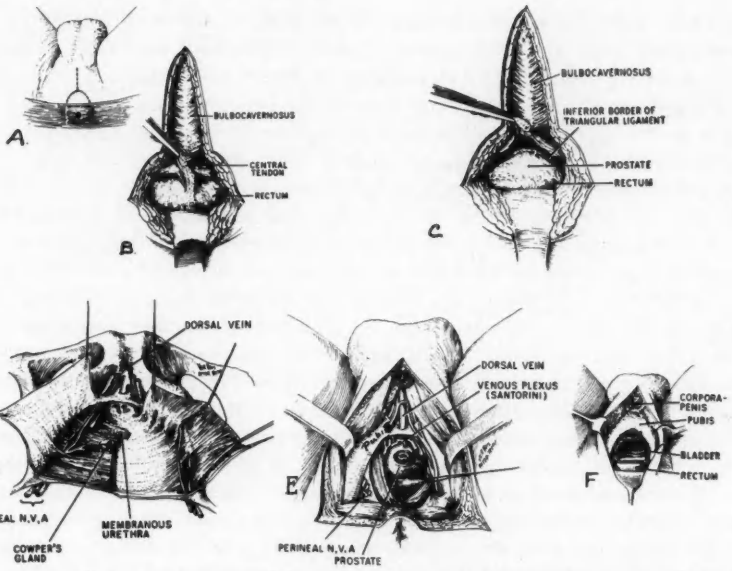

FIG. 5. Anatomical factors associated with removal of bulbomembranous urethra. *A*, perineal portion of incision. Note use of O'Conor shield for aid in localizing rectum. *B* and *C*, separation of rectum is carried out as for perineal prostatectomy. *D* and *E*, anatomical features of triangular ligament and its contents. These must be removed and bleeding controlled. *F*, appearance after such removal with prostate also removed. Remainder of bladder can be used for cystostomy drainage or can be removed from above when pelvic lymphatics are treated.

cated as far as the local removal of the tumor is concerned (fig. 5). Certainly coagulation through an external urethrotomy is of no avail, and in cases involving the prostatic urethra, local transurethral resection and coagulation except in very superficial tumors will not give satisfactory results. In one of our cases, the tumor arose primarily in the prostatic urethra and transurethral resection and coagulation of the tumor were carried out. No irradiation therapy followed this treatment, and it did not result in cure. It would seem that radical prostatectomy and urethrectomy with local removal of the regional lymph nodes would be the treatment of choice, and if such a radical procedure is not indicated, then local transurethral coagulation with intraurethral irradiation of some type should be done. Prostatectomy would not ordinarily suffice in these cases because the membranous urethra is usually involved, necessitating its removal together with the bulbous urethra in one mass. Diversion of the urine is effected by suprapubic cystostomy, cutaneous ureterostomy, or ureterocolostomy.

Radiation therapy for the local destruction of carcinoma of the male urethra has rarely been used. It was not used at all in any of our 6 cases. It was only used three times for tumors of the anterior urethra and four times for those cases involving the posterior urethra in the series collected by Kreutzmann and Colloff. In two of these it produced satisfactory local destruction of the tumor, but

as I have indicated previously, logically it would seem that surgical removal can accomplish more and with greater certainty than local irradiation. Irradiation may be of value as an adjunct, however, in selected situations.

Before considering the management of the lymphatics, it is well to describe some points with regard to the lymphatic spread of cancer emphasized by Willis[7] in his studies of this subject. He states, "The spread of cancer cells by their growth as cords in the lumina of lymphatics is an unusual phenomenon in cases of operable cancer, and when it does occur the permeation is generally only of microscopic extent. In other words for operable cases of cancer, embolism is the only important type of lymphatic spread. Even in advanced cases with multiple glands affected, it is likely that embolism from gland to gland is largely responsible for the affected glands which may at first be discrete and unconnected. Later, however, adjacent glands become bound together by tumor-occluded lymphatics and infiltrated, extracapsular tissues." The second point which he makes is also of importance in consideration of the operability of the tumor: "Extensive lymphatic permeation is rarely or never a simple centrifugal process, but depends on confluence of separate zones of permeation from subsidiary foci in regional nodes established by metastases." These principles are useful in consideration of the type of operative procedure to perform with regard to the lymph nodes. Large masses of nodes mean retrograde lymphatic permeation and embolization with practical certainty of inoperability. On the other hand, local apparent operability may be associated with embolism to regional nodes which may satisfactorily be removed without block dissection to the original tumor. In other words, it would seem perfectly logical in instances involving cancer of these areas where local infection with infected regional lymph nodes may play a great part in confusing the issue with regard to involvement of the regional lymph nodes and in the repair of the wound following removal of these lymph nodes, to simply remove the tumor locally first and at a secondary stage after the local operative wound has healed to remove the regional lymph nodes.

The lymphatics[8] of the male urethra consist essentially of a lymphatic capillary network which extends throughout the entire length of the urethra developing from behind forwards. This is particularly abundant in the region of the fossa navicularis. These lymph vessels, according to Sappey, are united by multiple, transverse and oblique anastomoses. The network is continued posteriorly with that of the ejaculatory duct and the bladder, and anteriorly with that of the penis. This network empties into a group of collecting trunks which Poirier and Cuneo divide into four groups, those of the glans, those of the pendulous portion of the urethra, those of the bulbomembranous portion of the urethra, and the prostatic portion. Let us note before going ahead with the description of the various collecting trunks and the location of the regional lymph nodes that this capillary network may be the pathway for spread posteriorly from the more anterior portion of the urethra of tumor by local extension when collecting trunks leading to the inguinal nodes are blocked not only by tumor but also by

[7] Willis, R. A.: Pathology of Tumours. St. Louis, Mo.: The C. V. Mosby Co, 1948.
[8] Tobias, M. J.: The Anatomy of the Human Lymphatic System. Ann Arbor, Mich.: Edwards Bros. Inc., 1938.

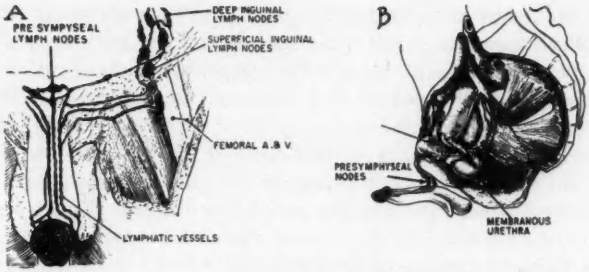

FIG. 6. *A*, lymphatics of penile urethra. Note particularly presence of presymphyseal nodes. (After Testut.) *B*, lymphatics of bulbous and posterior urethra in male. Note extensive drainage to presacral nodes and nodes along external and internal iliac arteries.

the results of extensive infection. It then may well be that the tumor cannot spread by embolism to the regional nodes and must spread posteriorly, and therefore spread upward along the prostatic urethra, the base of the bladder and about the bladder into the pelvis.

The urethral collecting trunks in the region of the glans traverse the urethral wall on each side of the frenulum and are continuous with the collecting trunks of the glans which ascend along the prepuce to terminate with the latter. These form three or four dorsal collecting trunks which are carried backward (as illustrated in figure 6, *A*) under the fascia and along the deep dorsal vein towards the root of the penis. At the root of the penis they may terminate in a presymphyseal lymphatic plexus where there may be several intercalating nodules. From this plexus the lymphatics spread laterally to the region of the femoral canal emptying into the inguinal nodes.

The collecting trunks of the penile urethra appear on the inferior surface of the penis, soon around the corpora cavernosa and then travel with the collecting trunks of the glans terminating, as described above, in superficial inguinal, deep inguinal, femoral and even in the iliac nodes.

The collecting trunks of the bulbomembranous portion of the urethra may be divided into three groups of collecting vessels. One of these emerges from the superior surface of the bulbous portion of the urethra and follows the course of the urethral artery or the artery to the bulb and in this manner reaches the trunk of this blood vessel. The second collecting vessel ascends behind the symphysis pubis to terminate in the medial retrofemoral node. The third collecting vessel comes chiefly from the membranous portion of the urethra and is carried from below upward in front of the prostate and bladder and unites with the lymphatics from the inferior part of the anterior vesical wall, terminating in the retrofemoral and iliac lymph nodes. The lymphatics from the prostatic portion of the urethra are similar to those of the prostate and are illustrated in figure 6, *B*. It will be noted particularly that one group involving the apex of the prostate in the membranous urethra passes posteriorly to follow the vessels through Alcock's canal back to the hypogastric nodes.

Taking into consideration the underlying general principles of lymphatic

metastases, as described by Willis and others, and the anatomical considerations of the lymphatic spread from the various portions of the urethra, as just reviewed, how are we to manage the problem of the lymphatics in these patients?

It is obvious, as emphasized by Hotchkiss, and also according to the studies of Willis, that a locally operable lesion may be completely removed surgically and yet have embolic involvement of the regional lymph nodes. In the anterior portion of the urethra involving primarily the pendulous, glandular and distal portions of the bulbous urethra, the lymphatic drainage for all practical purposes is primarily the nodes in the inguinal region and in the region of the femoral canal. Local surgical excision of the lesion, followed by block dissection of these regional lymph nodes on both sides, either at the same time as the original operative procedure is carried out, if very little infection is present, or as a secondary procedure following complete healing of the original lesion may be carried out in individual cases. It might be wise at the time that this procedure is carried out, to remove or at least study the iliac nodes lining the pelvis and the hypogastric nodes, since embolic involvement of some of these nodes may be present and they can readily be removed during the operative procedure (fig. 7).

If the original tumor involves the bulbous and membranous and prostatic portions of the urethra, exploration of the iliac and hypogastric nodes and their removal if involved are mandatory since more direct drainage to these areas as present in such cases, and they cannot be watched clinically.

When a good deal of local infiltration is present, usually associated with infection, irradiation therapy of the regional lymph nodes should be given serious consideration. It may also be of value in those instances where it is quite likely that no gross metastases are present, and it would seem that the radical lymph

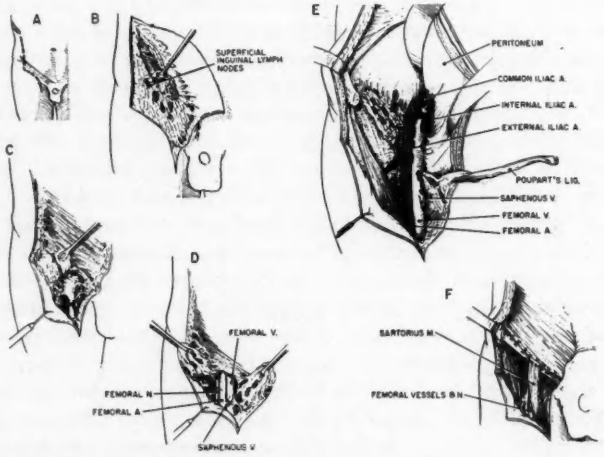

FIG. 7. Diagrams illustrating one type of surgical approach to inguinal and pelvic lymph nodes. Note disposition of inguinal ligament.

TABLE 6. *Carcinoma of the female urethra: Treatment and results by various authors*

Author	Treatment	No. of Cases	No. of Cases Well
Fricke & McMillan	Radiation	24	7
Fricke & McMillan	Local excision + radiation	11	8
Sparks & Parsons	Various types	119	15
Taussig	Radiation	12	1
Taussig	Local excision + adenectomy	3	3
Taussig	Local excision alone	1	0
Auer	Local radiation + excision	14	6
Auer	Local radiation + excision + adenectomy	6	3
Kieth	Local radiation	3	3
Kaplan	Local radiation	2	1
Kaplan	Local radiation + local surgery	2	2
Kaplan	Local radiation + x-ray to nodes	1	0
Ritter	Radical surgery	9	5
Ritter	Radiation alone	11	0

TABLE 7. *Carcinoma of the female urethra: Recommended therapy by various authors (after Ritter[9])*

Radical surgery locally and regional nodes	10
Radium + local surgery or coagulation + x-ray to nodes	10
Radium for primary + surgery to nodes	6
Local surgery and radium—nodes?	2
X-ray therapy to local and nodes	1
None satisfactory	2

node dissection would not be worthwhile; or in those instances where lymph node metastases are quite sure to be present and, for one reason or another, operative removal is not indicated. Hotchkiss has shown that these tumors are frequently fairly radiosensitive, and it may very well be that for all practical purposes, the metastases to the regional lymph nodes can be destroyed or their growth slowed down tremendously by intensive x-radiation. When one considers x-radiation it is important, as can be seen in figure 6, *A*, to give this therapy, not only to the inguinal nodes, but also the hypogastric and iliac nodes and also the nodes in the region of the symphysis itself.

There is some question as to the relative incidence of embolic phenomena and metastases to the regional lymph nodes. Hotchkiss feels that this is much more common than we are ordinarily given to believe. On the other hand, the results of the cases collected by Kreutzmann and Colloff would seem to indicate that marked regional lymph node involvement comes on relatively late in the course of the disease. However, for the most part, these cases come to us late and therefore serious consideration must be given to the regional lymph nodes and lymphatics.

[9] Ritter, D. W.: Primary malignancy of the female urethra. West. J. Surg., **61:** 420–429, 1953.

TABLE 8. *Carcinoma of the female urethra: University of Iowa Hospitals, 1935–1955*

No.	Case	Treatment	Remarks	Result
1	E. M.	Local excision	Local recurrence treated with x-ray	Death
2	N. C.	Radium needles 2736 mg. hrs.	Local recurrence + metastasis	Death
3	J. C.	Local x-ray, 2000 R		"Cure"
4	N. H.	Local radium + x-ray treatment 2400 R		Death
5	B. H.	Local x-ray	Very extensive when seen	Death
6	R. K.	Local radium + x-ray	Very extensive when seen	Death
7	A. M.	Radon seeds + x-ray	No stricture, no incontinence	"Cure"
8	G. T.	Radium + 8000 R x-ray	Very extensive when admitted	Death
9	J. P.	Radium + x-ray	Very extensive when admitted	Death
10	L. A.	Local excision, coagulation, radium + x-ray, ureterointestinal anastomosis	Incontinence, lymph nodes not involved	"Cure"
11	B. R.	Local excision + coagulation	Incontinence	"Cure"

Carcinoma of the female urethra is a somewhat more common lesion than cancer of the male urethra. Moreover from the recorded experience its prognosis seems better than the corresponding lesion in the male which occurs in the bulbomembranous portion of the urethra. Also in contrast to the experience in the male, many more of these cases are treated by radiation therapy than by surgery (tables 6 and 7).

Fricke and McMillan[10] describe a group of 35 cases seen at the Mayo Clinic from 1918 to 1942. In 26 of these 35, enlarged inguinal nodes were present which means that the tumor has infiltrated the anterior vaginal wall. With radium alone, of the 35 cases, 14 were treated; two of these survived 5 years. Ten were treated with radium and x-ray therapy; five of these survived 5 years. Nine were treated with excision and radium; seven of these survived 5 years; and two were treated with excision, radium and deep x-ray therapy; one of these survived 5 years. The survival was approximately 28 per cent. E. W. Riches and T. H. Cullen[11] reviewed 28 cases. Ten of these were females and only one survived 5 years. They believe that distant metastases occur in one-third of all cases, and in 5 per cent metastases to the inguinal nodes are present.

In the 20-year period from 1935 to 1955, eleven cases of primary cancer of the female urethra were seen at the University Hospitals (table 8). The following forms of therapy were carried out: 1) local excision followed by deep x-ray therapy; 2) insertion of radium needles followed by deep x-ray therapy; 3) local

[10] Fricke, R. E., and McMillan, J. T.: Radium therapy in carcinoma of the female urethra. Radiology, **52:** 533–540, 1949.

[11] Riches, E. W. and Cullen, T. H.: Carcinoma of the urethra. Brit. J. Urol., **23:** 209–221, 1951.

FIG. 8. External appearance of case 1 of our female series. An epidermoid carcinoma of urethra which appeared operable. Surgical excision was tempered by attempt to maintain sphincter control. Local recurrence and then widespread metastasis.

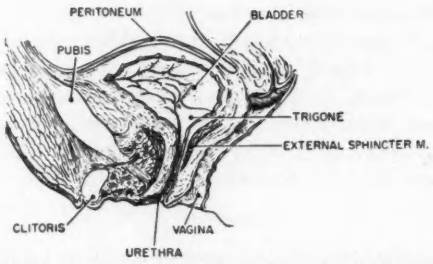

FIG. 9. Female urethra. Note location of sphincter musculature necessitating its sacrifice if radical destruction of tumor of any size in this location is to be achieved.

x-ray therapy alone; 4) radon seeds plus x-ray therapy; 5) local excision by the use of a high frequency current followed by x-ray therapy; 6) local excision and coagulation alone. Of these 11 cases, four have apparently been cured of their tumors. One had local destruction of the tumor by means of deep x-ray therapy alone. Another had local destruction of the tumor with radon seeds and x-ray therapy. The third had local excision followed by radium and x-ray therapy. The fourth had local excision and coagulation alone. Three of the four cases ended up with incontinence which was treated in one case by ureterointestinal anastomosis and in the other two by suprapubic cystostomy. In this series of the seven who died of the disease, four had such extensive cancer at the time they first appeared for therapy that it was quite apparent no type of therapy would be more than palliative. In the other three the lesions were apparently

operable or apparently destructible. In one local excision was carried out which was not done widely enough because an attempt was made to save the sphincter. Local recurrence and spread of the lesion followed. It is likely that a more extensive local excision with diversion of the urinary stream might have led to a different outcome. In the other two irradiation was carried out rather than extensive local removal, again in the hope of saving sphincter control. In both local recurrence and metastases occurred (figs. 8 and 9).

From a review of our own cases, it would seem that the therapy for carcinoma of the urethra in the female falls essentially into the following situations. If the lesion is very small and distal to the sphincter, a combination of local excision or local radium or radon seed application with deep x-ray therapy to the regional lymph nodes offers a good chance for local destruction of the tumor and a cure. However, in the majority of instances, this type of lesion is not present and therapy should be essentially the same as that outlined for carcinoma of the male urethra involving primarily the bulbomembranous portion. In other words, wide excision of the local lesion, diversion of the urinary stream to take care of the incontinence, and management of the regional lymph nodes are indicated in much the same manner as outlined for those individuals with carcinoma of the male urethra.

Palliative therapy is of course of use only in those instances where curative therapy is no longer possible due either to distant metastases or to extensive involvement. Palliative therapy consists essentially of diversion of the urinary stream by means of ureterointestinal anastomosis, cutaneous ureterostomy, suprapubic cystostomy, small doses of deep x-ray therapy to relieve pain, chordotomy to relieve pain from spread and metastases and other palliative measures which might seem indicated in the individual instance. It is necessarily highly individualized depending upon the local problem. Its principles are the same for tumors occurring in either sex.

SUMMARY

In summary, then, the treatment of carcinoma of the male and female urethra is described on the basis of results of therapy in the literature, in six male cases and eleven female cases seen at the University Hospitals in the period 1935 to 1955, and the anatomical, pathological and surgical considerations involved.

DISCUSSION

DR. THOMAS E. GIBSON (San Francisco, Calif.): I would like to emphasize two points in connection with carcinoma of the urethra. The first point relates to the x-ray diagnosis of the lesion, as revealed in this urethrogram. Note the widening of the bulbomembranous urethra to form a large cavity with irregular borders and radiating sinus tracts. The entrance and exit to this area of cavitation are constricted, rendering catheterization difficult. Such a picture is absolutely pathognomonic of the ulcerating type of carcinoma of the urethra, as differentiated from the fungating type and the annular constricting type. All three types are most often squamous cell carcinomas, as shown in the accompanying slides. Transitional cell papillary carcinoma and adenocarcinoma are comparatively rare.

The second point requiring emphasis relates to radiation therapy. The perineum tolerates deep x-ray therapy very poorly. Only moderate dosage may result in widespread sloughing of the perineum and even the adjacent rectum.

DR. LUIS A. SANJURJO (San Juan, Puerto Rico): I don't have an answer to explain whether malignant tumors of the urethra arise as a result of urethral strictures. It is curious enough, however, that in our series of 5 cases in Puerto Rico, all these patients had urethral strictures, and these were patients who had neglected at one time or another their strictures. All of these, with one exception, had multiple perineal fistulas and abscess formation.

Also, it is curious enough that strictures were present in 2 patients on whom we found extensive tumors in the posterior urethra and bladder. It is hard to ascertain whether or not the tumor developed first in the urethra and then extended to the bladder, or vice versa. We had only one case of malignant tumor of the urethra in a female patient. This was treated by ureteral transplants into the sigmoid and total cystectomy. That was 4 years ago and the patient is doing well.

DR. BEN D. MASSEY (Pasadena, Calif.): I haven't reviewed our records, but I remember briefly 3 cases of carcinoma of the posterior urethra that we have had; there are a couple of points which I think are of some importance. One is that the presenting symptom in two of these cases was hematospermia, which usually, I think, is considered a rather innocuous presenting symptom. The second feature of these 2 cases was that it was practically impossible to make a diagnosis by cystoscopic examination. The patients presented a diffuse granularity of the posterior urethra, which is a rather common situation. It took two examinations with biopsy before we made the diagnosis.

As to the ages of these two gentlemen, one was 51 and the other one approaching 70. The 51-year-old had a cystectomy and radical removal of the prostate, seminal vesicles and bilateral ureterosigmoidostomy, and did extremely well for 3 years. Incidentally, his ureteral transplants were working perfectly and he was doing heavy labor without any difficulty whatsoever. He illustrated a feature which Dr. Flocks brought forward, i.e., the importance of the lymph

drainage through the triangular ligament to the perineal vessels, by developing extensive carcinomatous plaques in his triangular ligament.

The other man had had a radical suprapubic prostatectomy, and he died some time later, apparently free of his disease.

The third patient had a rather small papillary carcinoma attached to the verumontanum, which was grade 3 on biopsy, and which was successfully destroyed locally by radon implantation.

We have had about three carcinomas of the female urethra. Two were small granularities presenting at the urethral meatus, which were quite successfully handled by radon implantation. The most recent was a woman of about 55, a school teacher, who was sent to us because of extensive bleeding, and the diagnosis had been made by a general surgeon who does cystoscopy. This was an extensive carcinoma involving the urethra, or at the level of the bladder neck, and it seemed that excision or radical approach would not solve the problem.

We removed the gross lesion transurethrally and then used quite an extensive amount of radon, undershooting through the urethra and around the bladder neck, and she returned some time later with an apparently satisfactory result. Twelve months later, there was no evidence of recurrence. This was a grade 3 type of carcinoma.

I would like to answer Dr. Thomas's question about what to do with the granularities and protrusions of the female urethra with bleeding. About 15 years ago, we stopped doing a lot of local treatment and found that most of those women have deficiencies of female hormone. Extensive granularity and bleeding are often more or less sympathetic responses to chronic vaginitis, pyogenic in character, and stilbestrol suppositories, in fantastically small amounts, control them without any local treatment whatsoever.

Dr. Gilbert J. Thomas (Santa Monica, Calif.): It is evident that there are few of these tumors seen in our patients at the present time. I would like to inquire of Dr. Flocks his method of handling nonmalignant caruncle of the meatus of the urethra in the female, by cautery or other means?

In my experience, these areas, when cauterized, are very painful afterward and you have a complaining patient on your hands, sometimes for months postoperatively.

I want to make a case report concerning a patient from the Veterans Hospital Clinic who had a cancer of the posterior urethra. This was published by Drs. Goodwin, Kaufman and Moore of our staff (Surg. Gynec. & Obst., vol. 97, Nov. 1953), but I think the technique used is unique and should be in this discussion as it illustrates some of the technical points discussed by Dr. Dean, Dr. Flocks, et al.

This 57-year-old white man entered the hospital with a 7-month history of dysuria, and a 6-month history of a tender perineal mass. Prior to his admission, biopsy of the perineal tumor performed by a colleague revealed grade 2 squamous cell carcinoma of the urethra. Suprapubic cystostomy had been performed for relief of severe obstructive symptoms. There was no history of gonorrhea or urethral stricture.

Examination revealed a firm, fixed, tender perineal mass 5 cm. long and 3 cm. wide. The mass *could not be felt on digital rectal examination*, and the prostate was of normal consistency and mobility. The suprapubic tube drained purulent urine, and Bacillus proteus was recovered on urine culture. A bloody, purulent urethral discharge was present. Regional nodes were not palpably enlarged. Laboratory studies were normal.

Chest films and excretory urograms were negative, and no evidences of bony metastases were seen on roentgenographic survey. Urethrograms revealed an irregular dilatation extending 6 cm. in the bulbomembranous urethra. Urethroscopy confirmed these findings, and the tumor appeared to extend proximally to a point just below the verumontanum. The bladder was free of tumor.

Young's operation, segmental excision of the tumor followed by reanastomosis, was originally planned in this case. However, the degree of involvement and extension proximally made such a procedure inadequate. Following a 6-day period of bowel preparation, the operation described was done on March 4, 1952. The penis was transected in its midscrotal region, and no evidence of tumor was seen. Biopsy just below the triangular ligament revealed gross and microscopic evidence of tumor extending upward into the apex of the prostate. Total prostatovesiculectomy was done in an effort to remove all carcinoma.

The problem arose as to the best way to manage urinary diversion. Three possibilities were weighed: Closure of the bladder neck with permanent suprapubic cystostomy, conventional transabdominal ureterosigmoidostomy either at this time or at a second stage, and transplantation of the divided trigone to the rectum.

The exposure following the extensive resection appeared to favor the last mentioned, and previous favorable experience with this type of anastomosis induced us to try it here. The transplant proved to be time-consuming and difficult technically because of the depth of the wound, but a satisfactory anastomosis without tension was achieved. The operating time was 5½ hours. The stump of the remaining distal penis was sutured to the inferior pubic arch, as described earlier. It was believed that should the penis fail to remain viable, it could be amputated subsequently with ease.

Urinary output through the rectal tube was good from the first postoperative day. On the third postoperative day a leak through one or both anastomotic sites was evidenced by the drainage of large amounts of urine through the perineal wound and the suprapubic cystostomy.

Gentle suction was applied to a small catheter placed in the perineal wound which gradually became dry. When the rectal tube was removed on the tenth postoperative day, the patient passed feces and urine per rectum with good anal sphincter control. The suprapubic catheter was removed 3 weeks postoperatively, and the suprapubic fistula and perineal wound were healed and dry on the twenty-fourth postoperative day.

Excretory urograms on the thirtieth postoperative day revealed no evidence of dilatation of the upper tracts and no extravasation at the sites of the anastomosis. The patient's blood chemistry studies remained normal throughout the

postoperative course. One year postoperatively the patient was well and had no complaints. However, he would not return for examination or x-ray study, and no venture can be made regarding his cure.

DR. HENRY MORTENSEN (Melbourne, Australia): I think this has been a very important symposium to draw to our attention again this seldom seen but very serious condition, and I would just like to comment on some of the difficulties of diagnosis from the few cases that I have seen.

Firstly, I am sure, in quite a few of the advanced cases, the original diagnosis is made of extravasation of urine. Two of the cases that I have seen first presented in this fashion, the final diagnosis being only made when the proliferation of the tumor was seen through the incisions that had been made to treat the extravasation of urine.

Secondly, I once had a case which presented with what was regarded as a small polyp in the anterior urethra, prolapsing through the meatus, with smooth surface and apparent peduncle, which on excision under local anesthesia was returned by the pathologist as carcinoma.

Lastly, I had another case of a gentleman of 65 who presented with symptoms of difficulty in micturition and the complaint that over the past 18 months or two years on such occasions as he did have an erection, it was a deviated one.

On examination, rectally, he appeared to have a frank carcinoma of the prostate, and on examining the penis, there were two lesions, one at the penoscrotal angle, and one behind the caput of the penis, and our first thought was that these lesions were in all probability secondary manifestations from the carcinoma of the prostate.

However, under estrogenic therapy for a period of 2 months, although his urinary symptoms cleared up, there was no change in the penile masses. Considering his relatively long history of 18 months to 2 years, we then regarded these as Peyronie's disease. They were subjected to our standard treatment of large doses of vitamin E and radiotherapy.

The proximal one at the penoscrotal angle retrogressed to a degree in size and became softer. The anterior one behind the caput of the penis increased in size. At that stage we thought we had better do a biopsy. The report was carcinoma of the urethra.

DR. RUBIN FLOCKS (Iowa City, Iowa): (Closing) I want to thank the discussants and tell Dr. Thomas that for the most part, in patients with urethral caruncle, we hospitalize them, give them an anesthetic, and do surgical excision with a knife.

DR. WILLIAM P. HERBST, JR. (Washington, D. C.): (Closing) I have nothing further to say except that John Crenshaw many years ago devised a very ingenious instrument comparable to a hemorrhoidal clamp which allowed you to do away with a caruncle with trichloracetic acid which, in certain respects, does away with the problem of cicatricial reaction associated with electrical fulguration.

THE CURRENT STATUS OF THE CHEMOTHERAPY OF RENAL TUBERCULOSIS

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During the last 9 years, since the advent of streptomycin, we have been looking for some evidence of a new decline in the incidence of renal tuberculosis. It has seemed reasonable that with better control of pulmonary tuberculosis, we might, at about this time, expect to see some decline in the incidence of the blood-borne complications, such as renal tuberculosis. With that in mind, we have made a survey of the case material of the last few years, to see if we could detect any such decline. A review of the number of new cases treated in each of the past 5 years by the Veterans Administration, Army and Navy Cooperative Study revealed no significant decline.

We then checked the other sources of our material and found that the numbers of new cases at the pilot study unit at the Bronx Veterans Hospital again showed no significant decline in numbers of patients diagnosed during the past 5 years. In the year 1955, we have even seen an increase in the numbers of new cases diagnosed. We then checked the new cases at the Presbyterian Hospital in New York City, and again found no evidence of a decline during the past 5 years.

It may occur to you that we might have a large number of referred cases of renal tuberculosis at our hospital, because of our interest in this disease, and that they might distort our totals. However, all referred cases have been excluded from these figures on incidence. We have included only cases detected in local practice.

Only among children with tuberculosis (miliary and other) did we find a decline in the incidence of new patients with positive urine cultures for M. tuberculosis. On our pediatric urological service, we have seen no new cases of urinary tuberculosis in the years 1953, 1954, and 1955 whereas there were always a few previously. This decline has come since the adoption of "triple drug" therapy for miliary tuberculosis.

Over the past 8 years various chemotherapeutic regimens, using streptomycin alone, isoniazid alone, streptomycin plus PAS and the combination of streptomycin, PAS, and isoniazid, have been tested for effectiveness on groups of our patients with renal tuberculosis who were highly comparable in all respects. All patients were treated and followed on the same wards, by the same personnel, and under as closely similar conditions as possible during the 8-year period. It was recognized that these groups were not run as concurrent controls against one another, but they were run in serial fashion with the minimal possible interval between groups. These conditions were made necessary by the small numbers of patients available and by the discovery of new drugs as time progressed.

The severity of the renal lesions treated was highly comparable in each group of patients. All had renal lesions of moderately or far advanced cavitary type. Patients with minimal renal lesions (with no pyelographic cavities) were not included in these studies due to the fact that such lesions are so easy to arrest that they do not constitute a good test of the treatment. It was believed that the advanced lesions provided a much more rigorous test of the effectiveness of each regimen. It was also kept in mind that most of the renal lesions which are seen by the urologist are advanced lesions when first observed.

RESULTS OF TRIPLE DRUG THERAPY

The most effective drug regimen tested to date has been the combination of streptomycin 1 gm. twice weekly, isoniazid 100 mg. t.i.d. and sodium PAS 5 gm. t.i.d., all given simultaneously for one continuous year. Figure 1 shows a comparison of the results of treatment with three different chemotherapeutic regimens to date. It should be noted that the group of patients who received the triple drug regimen has shown no relapses of the urine cultures to positive, since the initiation of treatment. A group of 20 of these patients has completed 1 year of treatment plus 1 year of followup, at this writing. The fact that more relapses

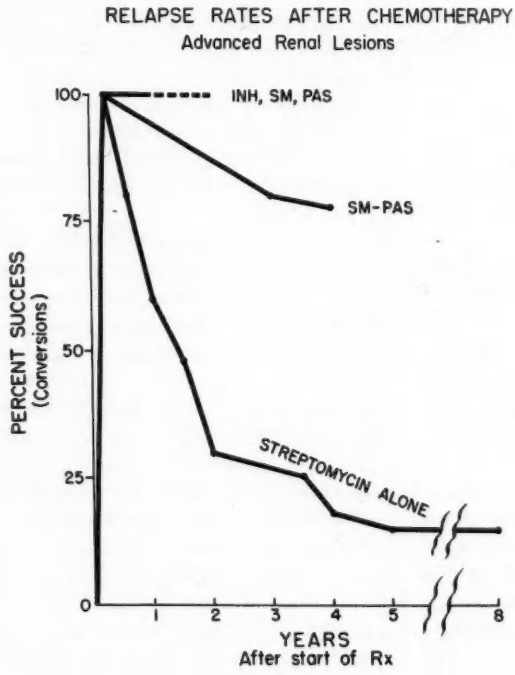

FIG. 1.

have not occurred by this time appears to indicate an advantage for the three drug regimen (isoniazid, streptomycin, PAS) over the two drug regimen (streptomycin, PAS). It is to be expected that some relapses will occur in the future, but none are apparent at this time.

Bed-rest, of a semi-ambulatory type, is considered an important adjunct during the first six to twelve months of this treatment. It is also important that the patients take full doses of the medications and skip no doses. It is our practice to give these patients therapeutic vitamin therapy throughout their treatment. This regimen has been so successful to date that we have not removed any tuberculous kidneys or portions of kidneys at the Research Unit for Genito-Urinary Tuberculosis in the past 3 years. One kidney was removed for study (see below). Should relapses occur, we will precede any surgical procedures with one month of isoniazid plus sodium PAS and follow the operation with eleven months of isoniazid and sodium PAS.

HISTOLOGY OF RESECTED LESIONS

One of our patients died of cardiac disease immediately after the completion of 1 year of triple drug therapy. At necropsy the right kidney was found to contain the expected scar at the position of his pyelographic lesion. Ureteral urine cultures from this kidney had been positive for M. tuberculosis prior to treatment. His voided urine had been repeatedly positive for M. tuberculosis before treatment. The urine cultures from all of these sources had become negative during and after treatment. On histological examination of the scar, the pathologist found no evidence of tuberculosis. No acid-fast bacilli could be grown from the kidney. A similar disappearance of the histological characteristics of tuberculosis has since been reported from England by Dr. Dick of the British Research Council. Four out of 25 of the kidneys which he examined showed a disappearance of the tuberculous histology after chemotherapy.

In another of our patients, who had received triple drug therapy for 1 year, the kidney was removed for pathological examination, upon completion of treatment. Prolonged attempts were made to grow M. tuberculosis from the massive caseous kidney lesions by Dr. Gladys Hobby of the Pfizer Chemical Co., who has been so successful in culturing viable tubercle bacilli from resected lung lesions. No growth has been obtained by Dr. Hobby, from these kidney lesions, at the end of 6 months. The histological characteristics of the far advanced lesions in this kidney showed a tendency toward healing but not complete disappearance of the changes due to tuberculosis. The pathological examination of this kidney was done by Dr. Oscar Auerbach of the Veterans Administration Cooperative Study. He suggested that further chemotherapy (18 to 24 months) might permit healing to become complete.

Streptomycin 1 gm. twice weekly, plus sodium PAS 5 gm. t.i.d. (two drug therapy) given together for 1 year proved much more effective than therapy with streptomycin or isoniazid alone, with only 20 per cent relapses after 4 years of followup. It did not appear to matter whether the 1 gm. of streptomycin was given daily or twice weekly, in combination with 5 gm. sodium PAS daily.

Giving streptomycin twice weekly was so much less toxic, and deferred drug resistance so well, that this dosage plan is now used. The factors that favored relapse in this group were: 1) less than one year of therapy; 2) older age of the patient; 3) coexisting pulmonary tuberculosis; 4) organisms already resistant to streptomycin due to prior treatment.

It was noted that prostatic tuberculosis responded to chemotherapy just as well as did renal tuberculosis.

CLORPACTIN FOR TUBERCULOUS BLADDER ULCERS

A new drug, "clorpactin 90," has been found effective in ameliorating the symptoms from tuberculous ulcers of the bladder. This is a topical medication which has a detergent action on the ulcers and also releases chlorine (as hypochlorous acid) in concentrations which are tuberculocidal. The symptoms from chronic tuberculous cystitis were markedly improved in most cases by the use of this medication as a bladder irrigation. These irrigations were moderately irritating, and had to be given several days apart.

INADEQUATE STERILIZATION OF CYSTOSCOPES

It was discovered that conventional methods used for "sterilizing" cystoscopes did not kill M. tuberculosis within one hour. Formalin vapor cabinets were unsafe (formalin vapor cabinets did not even kill B. proteus in 1 hour). Also solutions of mercuric oxycyanide, the quaternary ammonium compounds, and soaps were found unsafe for sterilizing cystoscopes which had been used on tuberculous patients. It therefore appeared conceivable that cross contamination between patients might occur if a cystoscope were used on a tuberculous patient and then used again on a clean patient within one hour. It was demonstrated, by our tests, that immersion in a 10 per cent formalin solution for a period of 5 minutes would kill M. tuberculosis on cystoscopes, provided that the cystoscopes had been washed with soapy water previously and that all stopcocks and lumina were open. It did not harm the cystoscopes. If formalin is objectionable, for any reason, the instrument germicide manufactured by the Lehn and Fink Co. has been found to be effective in killing M. tuberculosis if the cystoscopes are immersed in it for 1 hour. All of the solutions had to be washed from the cystoscopes so that they would not irritate the tissues of the patient. It was found that catheters and other instruments which could be boiled for 5 minutes were best sterilized by this method.

SUMMARY

Triple drug therapy (isoniazid, streptomycin and sodium PAS), given for 1 year, appeared to be more effective than double drug therapy (streptomycin plus PAS), in the treatment of renal and prostatic tuberculosis, and is our current treatment regimen. Bed rest, plus a high vitamin intake, were combined with the chemotherapy. Prolongation of the treatment to 18 or 24 months may be even more effective. To date, no new decline in the incidence of renal tuberculosis has been observed, despite the advent of chemotherapy.

Chlorpactin was found to be an effective new topical medication for tuberculous ulcers of the bladder.

Immersion of clean cystoscopes in a 10 per cent formalin solution for 5 minutes proved to be an efficient and harmless method for sterilizing instruments contaminated with M. tuberculosis.

We wish to acknowledge our indebtedness to our bacteriologists, Dr. Michael Kenney and Mr. Goldman, to our head nurse Miss Lydia Sechler, to our secretaries Mrs. Barbara Schindler and Mrs. Anne Machino and to the members of the Departments of Urology, Radiology, and Pathology of the Kingsbridge Veterans Administration Hospital who have co-operated so well in this study.

SMOOTH MUSCLE REGENERATION IN REPAIR OF EXPERIMENTAL URETERAL DEFECTS: THE SIGNIFICANCE OF THE DOUBLE LUMEN

FRANK HINMAN, JR. AND RUDOLF OPPENHEIMER

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Regrowth of the ureteral wall after partial resection has been studied experimentally by several workers[1-7] to determine the conditions for repair in Davis' intubated ureterotomy. The mucosa is found to be replaced within a week, and the muscle within 4 to 6 weeks.

Recent experimental work in our laboratory[8] indicated that actual growth of smooth muscle can occur, especially from the cut edges, although reconstitution is probably hastened by fibrous contracture of the scar tissue. Since the present report is on a continuation of that study, the principles and technique will be reviewed:

In order to separate the force of circular contracture of the fibrous tissue which is initially laid down to bridge the defect, from the factor of actual new growth of smooth muscle, a wire mesh fixed in a polyethylene splint (fig. 1) was laid across the cut edges. This prevented fibrous contracture, so that any muscle found beyond the barrier at the end of the experiment would necessarily have arrived by actual regeneration of the muscle fibers.

Sections made after from 6 to 12 weeks showed varying degrees of new muscle growth, but in all specimens in which the initial area of regeneration could be identified, it uniformly lay adjacent to the normal muscle on the other side of the barrier (fig. 2).

PRESENT EXPERIMENTAL STUDY

An incidental observation in the previous experiments was that fibrous tissue would grow along the barrier in certain instances, thereby forming a double lumen. Specimens showing this phenomenon form the basis for the present study.

Supported by the Edwards Fund for Medical Research.

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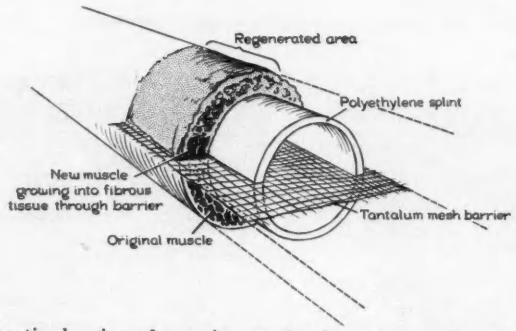

FIG. 1. Schematic drawing of experiment, showing relation of normal smooth muscle to newly regenerated muscle. Fibrous contracture is prohibited by wire barrier. Stippled area is site of: 1) excision of ureteral wall; 2) laying down of initial fibrous tissue, as normal step in healing process; and 3) ingrowth of smooth muscle from cut edges.

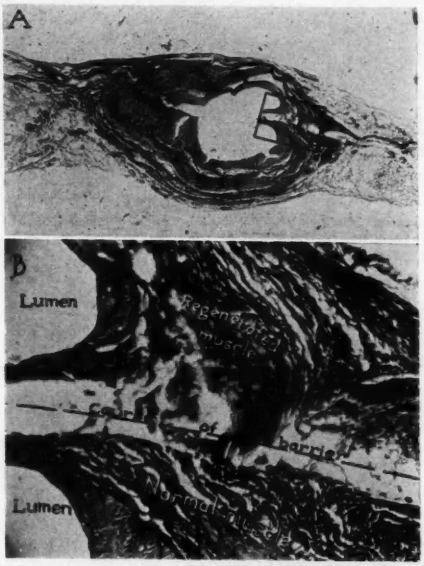

FIG. 2. *A*, cross section of ureter, No. 86E, 11 weeks after operation. Site of barrier is seen in *B*, with normal muscle below and tongue of new muscle growing into fibrous tissue above.

TABLE 1

Degree of Smooth Muscle Regeneration	Dog #	Weeks P.O.	Remarks
Minimal (±)	165	6	
	200	8	Ureter fell entirely away from splint
Moderate (3+)	110	9	
	86C	11	Control area with partial formation of double lumen
Complete (4+)	176	8	
	14	8	

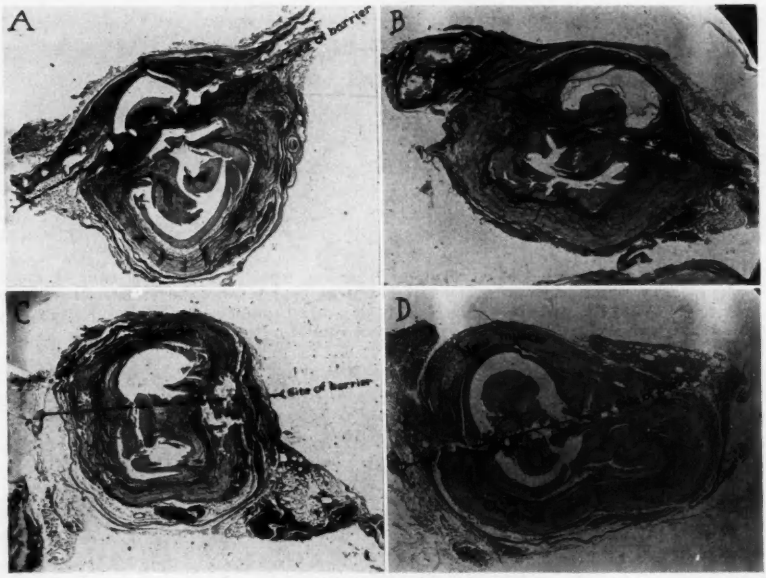

FIG. 3. Cross sections of ureters with incomplete double lumens. *A*, No. 165A; *B*, No. 110; *C*, No. 176 and *D*, No. 14. Note absence of new smooth muscle in *A*, but ingrowth of muscle in *B*, into new wall and into area of barrier.

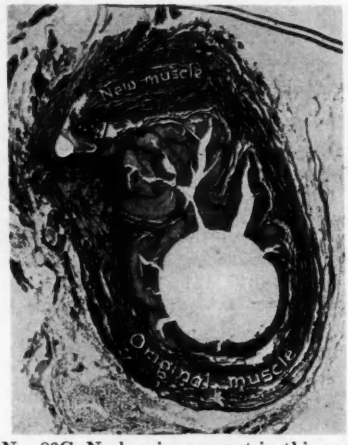

FIG. 4. Cross section, No. 86C. No barrier present in this area but ureteral mucosa and wall have fallen partially away forming a redundancy (early double lumen formation).

Six specimens were prepared by the technique described in the earlier communication, and representative cross sections studied. All ureters had two lumens on section (table 1). In four specimens (165, 110, 176, and 14), the double lumen resulted from growth of the initial fibrous tissue along the wire barrier. Epi-

thelium lined the outer lumen and smooth muscle grew into the new wall in varying degrees (fig. 3). Of significance is the fact that it grew also, although to a lesser degree, into the fibrous tissue lying across the wire barrier (fig. 3, *B*).

In one specimen, 86C, the wall of the defect had been drawn partially away, so that a sacculation was formed (fig. 4), a transition stage to true double lumen formation. However, because the margins of the cut ureter remained open, new muscle growth continued from the cut edges.

One specimen (No. 200) showed the most complete luminal reduplication. The ureter, after one-half its wall was resected, did not remain in apposition

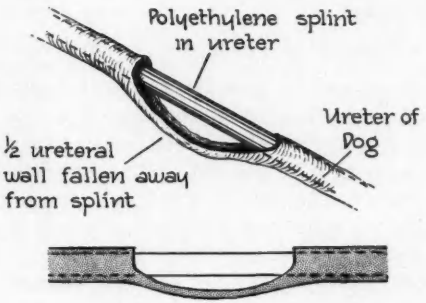

FIG. 5. Mechanism by which hemisectioned ureter falls away from splint, allowing healing as two separate tubes.

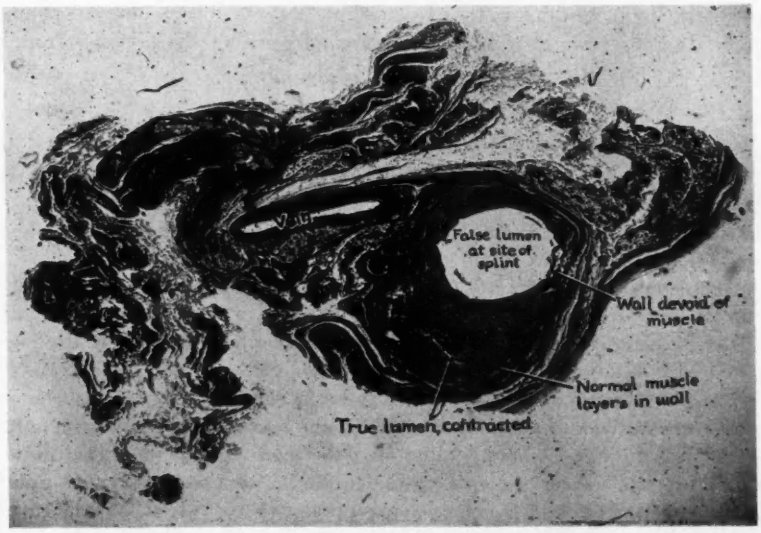

FIG. 6. Cross section of specimen No. 200. False lumen has been created about splint, leaving cut edges of ureter to draw together and reconstitute original lumen. Note that new ureteral wall is devoid of smooth muscle, apparently since a free cut edge of ureteral muscle was not present from which growth could start.

with the splint, but fell away (fig. 5). Its cut edges then simply reapproximated themselves leaving a slight scar and a small lumen. The significant fact is that no muscle is seen in the walls of the new "ureter" (fig. 6). The bundles of the normal ureter pursue their usual course without deviation or extension into the area of the new lumen. The meaning of the absence of muscle growth under these conditions is the subject of this discussion.

The question was raised during our studies as to whether the double lumen was actually a second ureter or merely one of the cystic spaces described by Trautner and Raaschau.[5] However, in the present experiments, the lumen was determined to be continuous with the ureter by dissection, since the splint in each case was withdrawn from the lumen.

SUMMARY OF EXPERIMENTAL FINDINGS

Smooth muscle can be seen to grow from the cut edges of the ureter when circular contraction is prevented by interposition of a wire barrier. Similarly, even if fibrous tissue grows across the barrier, forming two lumens, the muscle grows (although at a slower rate than the epithelium) into the septum.

If, however, the open hemisection of ureter falls away from the splint, its edges coapt, reforming the cylindrical structure, as would be expected from the experiments of Davis and others already cited. The adjacent fibrous tissue forms a sturdy wall about the nearby splint, but this new "ureter" is not invaded by smooth muscle bundles.

The formation of a second ureter has been described before as a complication of experimental intubated ureterotomy. However, double lumen formation provides an important link in the evidence that the site of regeneration of smooth muscle after resection of a part of the circumference of the ureter is from the cut edge of normal ureter.

SUMMARY AND CONCLUSIONS

An experimental technique was used to prevent healing by fibrous contracture of the ureteral defect in intubated ureterotomy, by interposition of a wire barrier. Actual smooth muscle regeneration has been observed and recorded.

Partial reduplication of the lumen occurred if fibrous tissue grew along the barrier. The septum was invaded by smooth muscle.

A complete second ureter was formed in one experiment in which the unroofed ureter fell away from the splinting catheter. The wall of the false lumen about the splint contained no muscle, the ureteral edges having healed together, leaving no exposed edge of muscle. Since no source for regeneration of new muscle was provided and no muscle growth occurred, there is reason to believe that smooth muscle regeneration after intubated ureterotomy occurs principally from normal ureteral wall. Perhaps it might follow that the more normal the initial ureteral musculature, the better the quality and quantity of the regenerated muscle.

These experiments add evidence to our previous observation that the smooth muscle of the ureter regenerates, arising in the main from the cut edge of normal muscle.

IS CYSTITIS CYSTICA AN INNOCENT OR A MALEFIC LESION?

REED M. NESBIT

The discovery of small cysts in the urinary bladder is a commonplace occurrence. Most urologists ascribe their presence to low grade infection and rarely treat the lesions specifically in the belief that they are themselves harmless and will disappear when the infection has been eliminated. In fact, they are rarely biopsied. Of course, all urologists are familiar with the reports of Stirling and Ash,[1-2] of Frank Patch[3] and others concerning the occasional occurrence of cancer in connection with cystitis glandularis, and perform biopsy in any case where there is any reason for suspicion.

The present report is made to point out that cystic lesions which are entirely innocent in appearance may in fact be composed of neoplasm and to urge that all such lesions be biopsied. The cystic lesions in question often have the appearance of small vesicles containing clear fluid while some have a yellowish or orange color and when punctured are found to contain rather thick xanthochromic material. They are rarely large, usually having a diameter less than 1 mm., and most of them are even smaller.

Most pathologists today accept the theory of von Brunn[4] that these lesions are the end product of metaplasia occurring in the transitional uroepithelium which starts as cell nests or epithelial buds. He believed that this proliferation of the epithelium was stimulated by inflammation and that the cyst formation was due to degeneration of the central cells of the nests. Today it is generally agreed that cell nests of Brunn develop as a result of chronic irritation, usually infection, but some investigations have suggested the possibility that toxins or other irritating chemical agents might provoke this type of proliferative change.

Whatever the cause, the lesions are generally seen in patients who complain of chronic, low grade bladder irritation, and infection is usually present in the urine. The experienced urologist who performs cystoscopy on such a patient will ordinarily find nothing to suggest that the cysts are anything but an objective manifestation of chronic infection and will perhaps be relieved not to have found anything of a more serious nature to treat. Of course, if ulceration of the mucosa is also present, he will be alerted to the possibility of concurrent neoplasm and will biopsy any such areas that arouse his suspicions.

The present report is concerned with a case in which typical cystitis cystica was observed in a patient who was examined by cystoscopy for low grade chronic infection. The curiosity of a urological resident physician rather than any sus-

[1] Stirling, W. C.: Cystitis follicularis, with discussion of other proliferative lesions of the bladder. J.A.M.A., **112:** 1326, 1939.

[2] Stirling, W. C. and Ash, J. E.: Pyelitis, ureteritis, and cystitis cystica, follicularis, glandularis and granulosa with a note on their pathogenesis. J. Urol., **45:** 381, 1941.

[3] Patch, F. S. and Rhea, L. J.: The genesis and development of Brunn's nests and their relation to cystitis cystica, cystitis glandularis and primary adenocarcinoma of the bladder. Canad. M.A.J., **33:** 597, 1935.

[4] von Brunn, A.: Uber Drüsenähnliche Bildungen in der Schleimhaut des Nierenbeckens des Ureters und der Harnblase beim Menschen. Arch. f. Micros. Anat., **41:** 303, 1893.

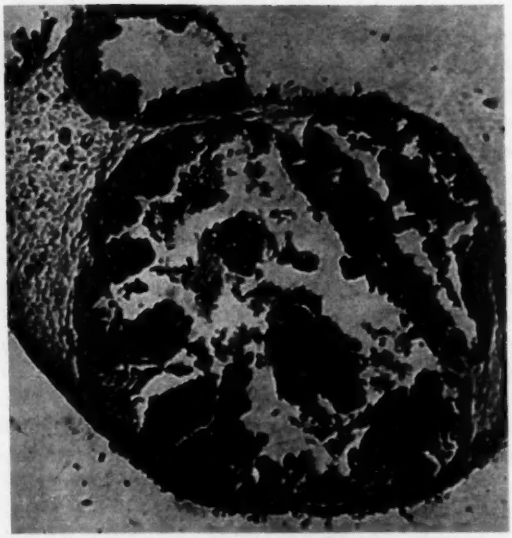

FIG. 1. Cyst removed at first biopsy. Low power. This demonstrates papillary neoplasms which are not invasive.

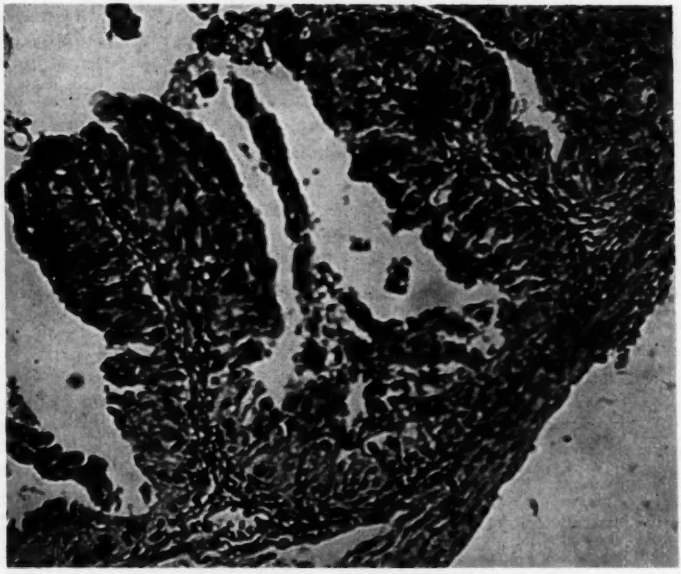

FIG. 2. High power of cyst removed at first biopsy

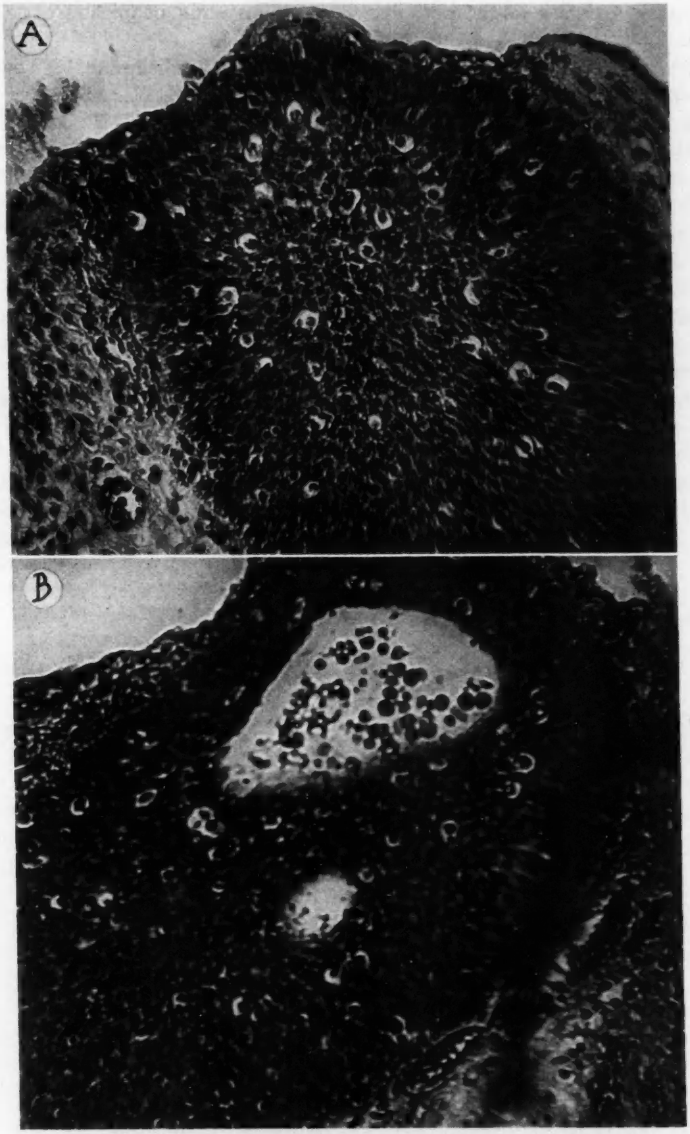

FIG. 3. A, typical cell nest of Brunn. Tissue removed at second biopsy. *B*, degenerating cell nest of Brunn; typical lesion of cystitis cystica.

picion of cancer led to the performance of biopsy and neoplastic disease was found.

The patient, U.M. No. 797504, was a 49-year-old Mexican laborer who complained of irritative bladder symptoms present for 5 months. These symptoms had become progressively worse, and at the time of admission he was incapacitated because of great pain on urination and voided every 15–30 minutes by day and seven to eight times at night. The urine contained only an occasional red blood cell and no white cells, and the stained sediment revealed numerous gram-positive cocci. The prostate gland was not enlarged.

Dr. James Morrow, first year resident on our urological service, performed a cystoscopy and found diffusely spread pustules throughout the bladder, but especially in the trigonal area. The intervening bladder did not appear especially abnormal. He was informed by his preceptor, who also looked into the bladder, that these were typical lesions of cystitis cystica, but in his inexperience he decided to find out how such a lesion would look under a microscope. He removed one of the cysts with a biopsy forceps, then went on with the completion of his retrograde study of the patient.

The microscopic sections reveal that the entire cyst was removed without distortion and that it contains several small papillary neoplasms which are not invasive (figs. 1 and 2). A few days later the patient was examined by cystoscopy,

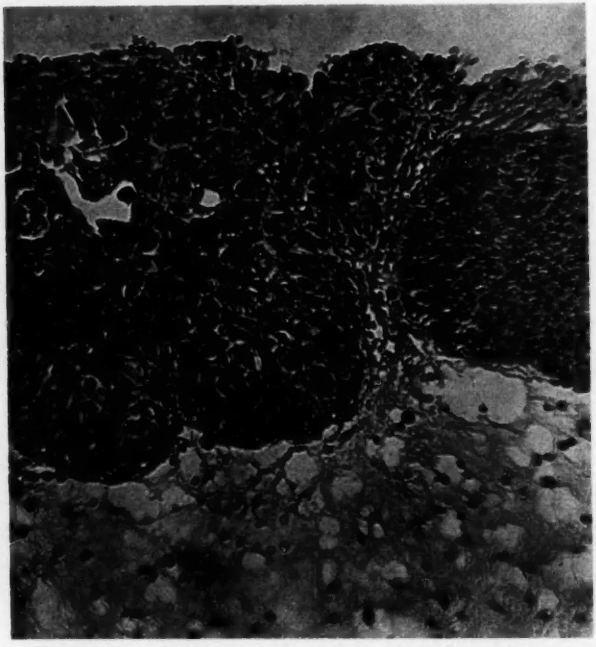

FIG. 4. Area of intramucosal carcinoma "carcinoma in situ"

and again the bladder was observed to have several typical lesions of cystitis cystica on and about the trigone. Again it was observed that there were no areas that in any way had the appearance of neoplasm. Further biopsy specimens of larger size were removed with the Lowsley cystoscopic rongeur. These specimens revealed a variety of lesions: some were typical cell nests of Brunn (fig. 3, *A*); some were typical of cystitis cystica (fig. 3, *B*); but there were several cysts in which neoplasm was present. Also, there were areas of the surface bladder mucosa which showed intramucosal carcinoma of the type generally termed "carcinoma in situ" (fig. 4). The involvement was so extensive on the bladder floor that it was felt that no treatment short of total removal would offer hope of cure and cystectomy was performed. Further microscopic study of the bladder revealed widespread involvement.

Certain features of this case have been of especial interest. They have provided us cause for reflection and have given your essayist a rude awakening concerning the malefic potentialities of cystitis cystica. I can well remember the time when, as a resident in urology, I first encountered lesions of this type. Prompted by curiosity regarding the composition of the pustule-like cysts, some of them were removed with biopsy forceps for microscopic examination. Some of them simply burst and exuded their liquid contents while others, more solid in character, proved to be cell nests like the lesions described by von Brunn. Since that early experience I must confess that I have never removed any more of the cysts for biopsy. To be sure, many cases which displayed this phenomenon have been biopsied when contiguous areas of the mucosa have appeared to be suspect and cancer has been observed in their vicinity on several occasions.

In the present case the enquiring resident surgeon had no reason to suspect neoplasm, and he removed only one lesion—a pustule-like cyst which he chose at random from several. Other, similar appearing lesions removed later from the same area were typical cell nests of von Brunn—some solid, some cystic—so the chance selection of a neoplastic cyst was entirely fortuitous. Had he picked one or more of the non-neoplastic cysts at the time of the first biopsy, cancer would not have been diagnosed or even suspected.

Another feature of the case which provides some cause for speculation is the finding of papillomas wholly within several of the cysts. This suggests the possibility that the factor which initiated proliferative changes in the epithelium was not infection, as appears usually to be the case when cysts occur, but perhaps a chemical carcinogenic agent. Several investigators[5-6] of these lesions in the past have suggested that toxins or other irritating nonbacterial constituents of the urine might provoke the formation of cell nests of von Brunn.

Certainly this unusual case has caused us to revise our attitude toward the lesions which we call cystitis cystica. It is our plan to take biopsies of several of the lesions whenever found, for they cannot be considered innocent until proven so.

[5] Giani, R.: Experimenteller Beitrag zur Entstehung der Cystitis Cystica. Centralbl. f. Allg. Path. u. Path. Anat., **17:** 180, 1906. Ibid p. 900.

[6] Herxheimer, G.: Uber Cystenbildungen der Niere und Abführenden Harnwege. Arch. f. Path. Anat., **185:** 52, 1906.

PAPANICOLAOU EXAMINATION OF URINE IN DIAGNOSIS OF URINARY CANCER: 2. FALSE POSITIVES IN DIAGNOSIS OF RENAL NEOPLASMS

HENRY M. WEYRAUCH AND JOSEPH C. PRESTI

From the Department of Surgery, Division of Urology, Stanford University School of Medicine, San Francisco, Calif.

One of the most difficult problems in urologic diagnosis is the detection of early neoplasms of the kidney. There is little difficulty in identifying obvious space-consuming lesions; when the diagnosis is not evident upon exposing the kidney at operation, biopsy can be safely performed if certain precautions are taken.[1] Difficulty arises in patients with obscure hematuria that may or may not be localized to one kidney when pyelograms are normal or reveal equivocal filling defects.

In view of the inadequacy of usual methods of diagnosis, it was our hope that the Papanicolaou technique, which has served so well in other fields, might

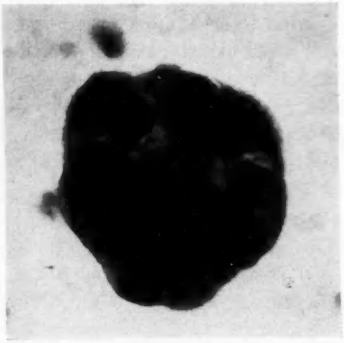

FIG. 1. Case 1. False positive smear of urine from left kidney. Cluster of cells contains enormous nuclei of different sizes and shapes.

be developed as a diagnostic aid in this type of case. However, the pitfalls of the method have proved so disconcerting that they warrant serious consideration. We have collected 4 cases in which false positive Papanicolaou smears, interpreted by pathologists experienced in the technique, contributed in part to the performance of nephrectomy for what proved to be benign lesions. A positive result is considered false when cytologic study shows what are thought to be neoplastic cells, but pathologic examination of tissue removed fails to confirm the presence of neoplasm.

In the 4 cases abstracted in table 1, hematuria was the presenting symptom. In two, bleeding was localized to one side of the upper urinary tract. In all in-

Supported by a State of California Department of Public Health Grant.

[1] Weyrauch, H. M., Wanless, H. L., Goebel, J. L. and Scott, K. G.: Biopsy of kidney for suspected neoplasm. J. Urol., **67**: 60–85, 1952.

FIG. 2. Case 2. Retrograde pyelogram demonstrating elongated cephalic calyx with irregularity of infundibulum. False positive Papanicolaou smear. Findings produced by hemorrhage and edema.

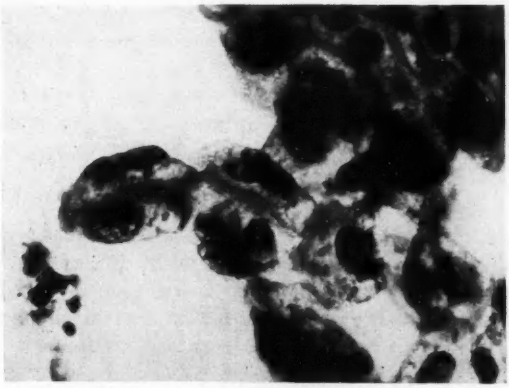

FIG. 3. Case 3. False positive smear from urine of right kidney demonstrating hyperchromasia, multinucleation and variability in shape of nuclei.

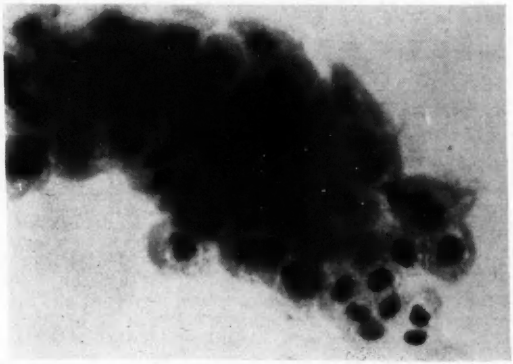

FIG. 4. Case 4. False positive smear of urine from right kidney showing cluster of well-differentiated cells with hyperchromasia and multinucleation.

TABLE 1. *Cases demonstrating false positive Papanicolaou smears of kidney urine*

Case No.	Sex	Age	Complaint	Urine	Cystoscopic Findings	Pyeloureterograms	Papanicolaou Studies	Operation	Pathologic Examination
1	M	27	Painless hematuria for 2 days	RBC ō WBC ō Bact. ō	Normal	Small, irregular filling defect minor cephalic calyx, left	Left kidney: Diagnostic of malignancy (fig. 1)	Left nephroureterectomy	Subacute papillitis, hyperplasia mucous membrane, cephalic calyx
2	M	43	Painless hematuria; left lumbar pain for 10 days	RBC++++ WBC occ. Bact. ō	Bloody urine from left ureteral orifice	Elongation and slight irregularity of infundibulum left cephalic calyx (fig. 2)	Left kidney: highly suspicious of malignancy	Left nephrectomy	Hemorrhagic papilla with edema, cephalic calyx
3	M	35	Painless hematuria and right lumbar pain for 10 days	RBC++++ WBC occ. Bact. ō	Bloody urine from right ureteral orifice	Small, persistent filling defect upper portion right renal pelvis	Right kidney: highly suspicious of malignancy (fig. 3)	Right nephroureterectomy	Arteriolarsclerosis with bleeding into renal pelvis
4	M	38	Microscopic hematuria for 9 months	RBC+ WBC ō Bact. ō	Normal	Small, persistent filling defect, minor cephalic calyx, right	Right kidney: strongly positive for malignancy (fig. 4)	Right nephrectomy	Normal kidney

stances, smears of urine obtained from the renal pelvis were reported as positive to highly suspicious for neoplasm after preparation by the usual Papanicolaou technique.[2] Pyelograms were either normal or demonstrated irregularities too minute to localize at operation. Following nephrectomy, pathologic examination of the operative specimens yielded the following findings: subacute papillitis, hemorrhagic edema of renal papilla, renal arteriolar sclerosis and normal kidney.

DISCUSSION

A review of the literature indicates that other workers have encountered a high incidence of false positive smears made from specimens of urine. In a series of 168 urologic cases, Chute and Williams[3] report 13 (12 per cent) incorrectly diagnosed as "positive" for urogenital cancer. Two patients of this false positive group were thought to have renal carcinoma; however, following operation one kidney was found to contain a benign cyst, and the other proved to be normal. McDonald[4] in 84 cases of suspected renal neoplasm obtained positive smears in 19; six (31 per cent) of these proved to be false positives.

Difficulties encountered in the application of the Papanicolaou technique to the urinary sediment in general and to the diagnosis of renal neoplasms in particular are:

1) The test is successfully applied only when neoplastic cells have been exfoliated into the urine. One is unable to obtain cells by scraping suspicious areas, as is possible in making smears from the cervix of the uterus. Despite the fact that fresh urine is examined, cells may have remained in the urinary tract for long periods, and frequently their nuclear and cellular structure cannot be adequately studied. Staining qualities are altered by the pH of the urine, the length of time cells remain in the urine after exfoliation and by the technique employed in preparing the smear (any drying before fixation exerts a deleterious effect).

Again, on some occasions, the exfoliated cells are so few that satisfactory interpretation is impossible. In a previous report concerning the use of the test in mass screening,[2] 22.2 per cent of the smears obtained from 1,575 individuals contained too few cells (less than six cells per smear) to allow intelligent interpretation. Furthermore, in recovering neoplastic cells from the upper part of the urinary tract, one is limited by the small amount of urine obtained by ureteral catheterization.

2) The nature of malignant lesions of the urinary tract limits use of the technique. The incidence of neoplasms of the renal pelvis is low. They constitute only 10 per cent of all renal neoplasms, yet these are the ones most likely to exfoliate. Most renal neoplasms are adenocarcinomas arising in the parenchyma. They do not invade the excretory tubules or renal pelvis to exfoliate cells into the urine until late in their development, usually after the occurrence of hematuria.

[2] Presti, J. C. and Weyrauch, H. M.: Papanicolaou examination of urine in diagnosis of urinary cancer. 1. As a test in mass screening. Trans. West Sect., A.U.A., **21:** 150–155, 1954; also J. Urol., **73:** 430–434, 1955.

[3] Chute, R. and Williams, D. W.: Experience with stained smears of cells exfoliated in urine in diagnosis of carcinoma of genito-urinary system. J. Urol., **59:** 604–618, 1948.

[4] McDonald, J. R.: Value of exfoliative cytology in genito-urinary and pulmonary disease. Am. J. Clin. Path., **24:** 684–689, 1954.

3) Many neoplasms such as papilloma of the renal pelvis exfoliate cells indistinguishable from normal transitional cells. Furthermore, well-differentiated, clear cell carcinomas of the kidney may fail to show cytological characteristics of malignancy. Papanicolaou[5] has called attention to the fact that cells with cuboidal or columnar form are often seen in ureteral smears in benign papillary growths. However, since they also occur in the absence of any growth their diagnostic significance is limited.

4) On the other hand, some normal cells of the ureter and renal pelvis closely resemble neoplastic cells. Whether actually exfoliated or separated from the normal mucosa by ureteral catheter, many of these cells vary considerably in size, form and structure, far beyond the range observed in other types of exfoliated cells.[6] The nuclei may have a fine chromatin network suggestive of proliferative activity. Nuclear enlargement alone, therefore, is not a valid criterion of malignancy in the ureteral specimen. An additional normal characteristic of cells in urine obtained by ureteral characterization is two or more nuclei. Papanicolaou[5] thought that giant, multinucleated cells are syncytia formed by a fusion of many cells, probably after exfoliation, since such cells are not seen in histologic sections of the ureter or pelvis; smaller, multinucleated cells are sometimes found in the renal tubules. Other possibilities are that the cells enlarge as the result of trauma during ureteral catheterization or from amitotic or mitotic division of the nucleus without a corresponding division of the cytoplasm.

5) Finally, atypical transitional cells with apparent hyperchromasia may be caused by inflammatory processes or renal calculi and lead to false positive interpretation.[5] These are small or medium-sized cells with deeply staining nuclei usually intermixed with inflammatory cells and erythrocytes.

CONCLUSIONS

In view of these considerations, when the Papanicolaou technique is applied to the diagnosis of neoplasms of the upper urinary tract, these precautions are essential:

1. Criteria of what constitutes neoplastic cells of the upper part of the urinary tract must be more stringent than criteria for cells obtained directly from tissue. Conclusive positive diagnosis should be based, not on one or two criteria, but upon as many neoplastic aberrations* as possible (fig. 5).

2) It is essential to make smears of the urine repeatedly. Interpretation should not be based on one examination alone.

3) Urine from the bladder should be examined as a control before obtaining specimens from the renal pelvis. Look with doubt on suspicious cells obtained from the renal pelvis when similar cells are not present in urine previously obtained from the bladder.

[5] Papanicolaou, G. N.: Atlas of Exfoliative Cytology. Cambridge, Mass.: Harvard University Press, 1954.

[6] Papanicolaou, G. N.: Cytology of urine sediment in neoplasms of urinary tract. J. Urol., **57:** 375, 1947; also J. Urol., **57:** 375, 1947 and Trans. Am. Assoc. Genito-Urin. Surg., **38:** 145–147, 1947.

*Criteria of malignancy: Marked nuclear enlargement, hyperchromasia, anisocytosis, anisokaryosis, multinucleation, crowding and engulfment.

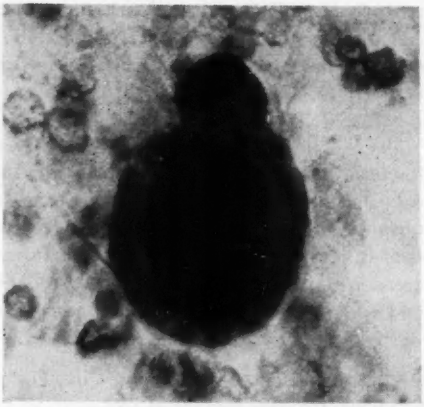

FIG. 5. True positive smear from urine of left kidney demonstrating cluster of cells with multinucleation, hyperchromasia, anisocytosis and marked nuclear enlargement. Left nephroureterectomy performed. Specimen showed small epidermoid carcinoma of renal papilla.

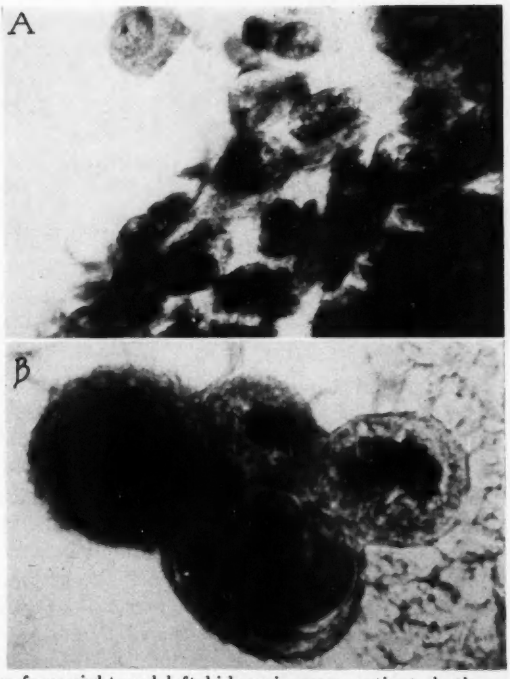

FIG. 6. Smears from right and left kidney in same patient; both are compatible with malignancy, but prolonged observation indicated they are both false positives. *A*, right kidney. Nuclei are large and hyperchromatic with prominent nuclear border. *B*, left kidney. Clump of cells demonstrates multinucleation, hyperchromasia and anisocytosis.

4) Urine should always be collected from both renal pelves for comparison (fig. 6). It is important to obtain urine not only from the side on which suspicion rests, e.g., when there is a pyelographic filling defect or bleeding from one kidney, but from the supposedly normal side as well.

SUMMARY

Four cases are presented in which Papanicolaou smears of urine obtained by ureteral catheterization were highly suspicious or positive for malignancy, yet careful pathological examination after nephrectomy failed to reveal evidence of neoplasm. Attention is called to the high incidence of false positive smears in the examination of renal specimens of urine, and other difficulties encountered in the application of the Papanicolaou technique to urinary sediment are discussed. Stringent criteria for positive interpretation are outlined.

The authors express appreciation to Drs. Alvin Cox, David Wood, Frederick Howard, Milton Rosenberg, Charles King and Eileen King for aid in the preparation of this paper.

DISCUSSION

DR. RICHARD CHUTE (Boston, Mass.): I am afraid this could not be dignified as a discussion, but I would just like to congratulate Dr. Weyrauch on his particularly good paper and say that I am in complete agreement with him. It is really thin ice, and you have got to walk carefully.

DR. EDGAR BURNS (New Orleans, La.): We see quite a number of cases of cystitis cystica, and have never considered it a lesion of any major importance. I should like to ask Dr. Nesbit if he considers it necessary to perform biopsy in any significant number of these.

DR. DONALD CHARNOCK (Los Angeles, Calif.): I was very much interested in this report of Dr. Nesbit's, because a few years ago, I had a nice lady in whom we found a large area of cystitis cystica in the bladder. We tried to destroy it by fulguration and local treatments, but it kept recurring. We had very competent consultation on this case, and the help we got was, well, "Keep fulgurating it; you will eventually get it completely destroyed."

Subsequently, definite papillary carcinoma could be observed in the upper area, which was proven by pathological examination. That was completely resected, and since that time this lady has had no further cystitis cystica, although we have been repeatedly examining her every three months.

DR. FLETCHER COLBY (Boston, Mass.): I would just like to add a word to Dr. Lattimer's very nice discussion of renal tuberculosis.

In our cases of renal tuberculosis at the Lakeville State Sanitorium in Massachusetts, we have felt that chemotherapeutic treatment should be carried on not for one year or two years, but indefinitely. We still don't know how many years may elapse before these patients will again have positive smears with a lesion that is off in the parenchyma of the kidney and has not healed. We base that on certain rather sad, unusual experiences. One was a woman who had her kidney removed 30 years previously for tuberculosis, was well in the meantime, very active, and 30 years later appeared at the sanatorium with tuberculosis in her remaining kidney, and no active focus of tuberculous disease elsewhere that we could detect.

Another was a similar situation in a woman who, 30 years later, came back after unilateral nephrectomy with tuberculosis in a remaining kidney.

So we feel that we don't know how long it may be before tuberculosis may appear from a sound area in the kidney.

DR. ORMOND S. CULP (Rochester, Minn.): I am very much interested in Dr. Lattimer's observations because we don't see very many patients with tuberculosis, but we see some very interesting ones.

I just want to mention one woman who had 4 years of medical treatment and was plagued with such horrible tuberculous cystitis that she was miserable. Her urine was negative and relief was obtained for the first time after bilateral partial nephrectomy.

We have had two patients who relapsed after a full year of medical management of their renal tuberculosis, but both had bizarre clinical problems and neither was treated exactly as Dr. Lattimer has just recommended.

DR. FRANK C. HAMM (Brooklyn, N. York): I congratulate Dr. Hinman on his ingenious method of demonstrating regeneration of the smooth muscle of the ureter. In our investigations we were able to demonstrate regeneration of the ureter without the use of splints or catheters. In some of our specimens the lumen appeared reduced in caliber, but adequate for drainage, as the kidney above the operated area remained normal.

DR. WILLIAM P. HERBST, JR. (Washington, D. C.): I would just like to comment on the general management of the tuberculous patient, along the lines that Dr. Thomas referred to many years ago, namely, the general build-up feature.

For many years, going 'way back to the time when Dr. Thomas was contributing in this field, it was my observation that these patients had a much better chance of becoming arrested cases in the presence of minimal lesions if they were kept on some preparation containing whole cod liver oil. At one time, at the City Hospital in Washington, there were three nurses with no demonstrable damage to the renal pelvis yet were carrying acid-fast bacilli on one side. They were kept a year on general rest and whole cod liver oil, and good dietary regimen. They eventually became arrested cases, and all three of them up to at least the last year have remained arrested.

I think we shouldn't lose sight of the general support aspect of these patients with renal tuberculosis, even though effective chemotherapeutic means of treatment are available.

DR. REED M. NESBIT (Ann Arbor, Mich.): May I ask Dr. Lattimer a question? What percentage or what proportion of patients on the triple medication are intolerant to taking the triple program?

DR. JOHN K. LATTIMER (New York, N. Y.): Occasional patients are intolerant of one or another of the drugs employed. These total some 5 per cent of our group. For instance, our women patients don't like the gastrointestinal symptoms from ordinary PAS, but they tolerate sodium PAS much better.

Patients in a group, in a sanatorium or on a ward where they are all taking the medications at the same time, will do better than they will at home. One of them may say "Well, if you can't take the PAS as pills, try it my way dissolved in bicarbonate solution and flavored a bit, or try another drug company's preparation."

I would say, as a rough guess, that we have no more than 5 per cent of our patients who will not tolerate the entire triple drug program. Of the drugs, I would say that PAS is the most troublesome. We have new anti-tuberculosis drugs under investigation, as you know, which may make it possible to devise a triple drug program of some sort for every patient.

We have given up the idea of giving a dose of PAS at bed time. That really upsets the patients. They cannot get back to sleep because of "gas" and diarrhea. We give the PAS after each meal rather than every 8 hours, because that is the only arrangement our patients will tolerate.

DR. GILBERT J. THOMAS (Santa Monica, Calif.): Certainly we should be very thankful for the way Dr. Lattimer has continuously informed us concerning his

clinical research regarding renal tuberculosis. He has had an opportunity of observing these patients until, as he described, "they get their last check from the government."

One routine I want to emphasize regarding treatment and that is that we still continue to employ hygienic treatment. I wish to emphasize the importance of the preparation of ureteral catheters and other instruments before cystoscopy. This technique is very important and when not used may interfere with the correct interpretation of the data obtained from the examination of the urine collected through the ureteral catheters.

We developed a technique which we believe is error-proof whereby the ureteral catheters were thoroughly cleansed mechanically; were autoclaved, and then were placed, not in a solution that would contain disinfectant, but in sterile water. When the ureteral catheters were passed through the catheter channels of the cystoscope, then the lumen of the bladder, they were constantly flushed with sterile water by means of a syringe attached to the catheter by well fitting adapters. We were dealing with a catheter that was sterile and that had not been immersed in a disinfecting solution. A few drops of a disinfecting solution collected with the ureteral specimen may negate your culture which otherwise might grow bacteria.

I would like to ask Dr. Nesbit if he has had an opportunity to re-examine, at autopsy or clinically, patients in whom cystitis cystica and other comparable lesions have been diagnosed and who have been under observation for long periods of time?

Dr. Nesbit: We haven't observed anything like this in our Department of Pathology before, if that answers your question.

Dr. Thomas: Have you had an opportunity to go back over your records and find out what happened to the individuals on whom a diagnosis was made of cystitis cystica?

Dr. Nesbit: No.

Dr. John K. Lattimer (New York, N. Y.): (Closing) With regard to Dr. Thomas's remarks about general hygienic measures for patients with renal tuberculosis, we certainly subscribe to the thought that one should "combine" or "add" chemotherapy to these old and well-established principles. We have been disappointed in the patients whom we treated on an ambulatory status because they had to go back to work making a living for their five children. They did not do so well as the ones who stayed right in the hospital during the entire year of treatment.

In regard to Dr. Thomas's point about discarding the first few drops of urine from the ureteral cultures, which are collected for ordinary pyogenic bacteria, I think that is very important, lest the sterilizing solution within the catheters fall into the culture tubes.

With regard to M. tuberculosis, however, we tried soaking our catheters in 1:1000 oxycyanide, but it didn't kill any tubercle bacilli; we got a lovely growth of tubercle bacilli after 24 hours' immersion in that solution, so that I suspect

that oxycyanide in the catheters would not interfere with the tuberculosis cultures.

Incidentally, we have been testing all of our ureteral specimens to see what the pH was. You know that there is a saying that tuberculous urine is classically acid. Well, from our observations it appears that the urine from a positive tuberculous kidney can be of any pH. The pH varied with the "alkaline tide," for instance, just as it did in any other patient. Therefore, a finding of "alkaline" urine does not preclude tuberculosis. This was true even of alkaline urine which contained no pyogens, so that the factor of urea-splitting infection did not enter.

With regard to the question about the sealed-off lesion out in the parenchyma, which might be reactivated years later, one of the objectives of our chemotherapeutic program is to see whether we can truly sterilize a sealed-off lesion. We are conducting experiments along those lines, and there have been some indications that with triple-drug therapy, we can sterilize some of them. And still other drugs, such as pyrazinamid, for instance (which is a potent anti-tuberculosis drug, but which is toxic for the liver) given in combination with isoniazid, have sterilized more experimental lesions than any other regimen. We are seeking ways to sterilize lesions at all times.

In regard to patients who fail to convert after chemotherapy, I believe that many of them failed to take full doses of the medications, or skipped doses, or failed to rest during treatment. If they do not take all the medicine, they don't get as good results.

Apropos of Dr. Culp's remarks about patients having multiple operations for renal tuberculosis (in his case, bilateral partial nephrectomy), we also have a patient who is a physician, whose renal tuberculosis did poorly after multiple operations.

Incidentally, I think renal tuberculosis is endemic among physicians, judging from the numbers of cases we have. I have the feeling—and it is a feeling I cannot prove—that perhaps over-long or repeated, or stressful operations, are very bad for these patients with renal tuberculosis. It might even be that chemotherapy alone would do better than chemotherapy plus surgery, because of the stress on the patient from over-vigorous surgical procedures.

I hope that answers all the questions. If anything comes up during the year that any of you would like to have investigated, in regard to renal tuberculosis, please let us know. We have a feeling of urgency about this study in that we have together a larger group of renal tuberculosis patients now than we will ever get together again, and if for any reason the Veterans Administration cannot support the work longer, or we cannot keep it up, we might lose this great opportunity to study renal tuberculosis further.

DR. FRANK HINMAN, JR. (San Francisco, Calif.): (Closing) I merely want to emphasize that what we reported this morning is only a small portion of the problem. We started back in 1951, and are still working, but I would hope that within the next four or five years we would have more evidence on things of im-

portance, such as drainage; the use of fat, as shown by Lapides; and other of the factors that are of clinical importance in the healing of ureteral defects.

DR. HENRY M. WEYRAUCH (San Francisco, Calif).: (Closing) To answer Dr. Culp, we are not totally ready to abandon the technique which I discussed today. Certainly if the diagnosis can be made by any other way, there is no use in carrying it out. But we all have those patients with obscure hematuria whom we worry about.

Once in a while you will get a little nest of cells by using this technique, and you can be absolutely certain of what you have; and in the occasional case it has a certain use. If we keep our eyes open, we can use it with safety.

DIAGNOSIS OF UROLOGIC COMPLICATIONS IN GYNECOLOGY

CARL RUSCHE

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The most common complications occurring during pelvic surgery on the female are the result of trauma to the urinary bladder or ureters. Injury to the bladder is often recognized at the time of surgery and repaired. When a urinary fistula develops postoperatively, a urologist may be consulted relative to the diagnosis and treatment; however, it is generally considered a gynecological problem.

The literature contains many reviews of the frequency of ureteral injury during extensive pelvic surgery. The incidence of this tragic happening is clothed by devious factors, so that many have been unreported, unrecognized, and often unrevealed because of the paucity of symptoms.

Since the generally accepted incidence of surgical injury to the ureter is relative and the arbitrary figure not entirely accurate, too great reliance cannot be placed on the frequency with which the condition has been encountered as a sequel of surgery. The occurrence of ureteral ligation as a complication of all operations on the female genital organs has been estimated as much as 3 per cent. The relative ratio of unilateral to the bilateral injury is presumed to be 6 to 1. The morbidity ratio of the past can be hardly comparable to that which existed prior to the institution of the various sulfa drugs and antibiotics; the complications, independent of infection, still tax the ingenuity of the surgeon and re-emphasize the great importance of all preventive measures. A decided interest has developed during the past years in a more general and better understanding of all the principles, which contribute to the prevention and correction of ureteral damage. Much of this has come about as a result of the experience of the war.

Abdominal surgical procedures have been regarded as the most frequent cause of ureteral trauma. However, the instances of injury to the ureter occurring during gynecologic operations have been more common recently due to the increasing use of panhysterectomy both in benign and malignant pelvic conditions.

The most common site for ureteral injury has been repeatedly noted by various surgeons. Novak described five danger zones in the female patient as follows:

1) Where ureter crosses the iliac vessels
2) Ovarian fossae
3) Intraligamentary portion of the ureter
4) Where ureter is crossed by the uterine artery
5) Intravesical ureter in the repair of vesicovaginal fistula

The most skilled and experienced gynecologist may inadvertently cut or ligate one or both ureters in a hysterectomy, if it is unusually complicated or difficult. The urologist is consulted when complete anuria or persistent flank pain follows such a procedure as removal of diseased fallopian tubes or intraligamentous

cysts, vesical tumor, or carcinoma of the uterus. The usual types of injuries are ligation, incision, resection, clamping and extensive stripping of the ureter with interference of the blood supply.

The general symptoms of rupture or penetration of the ureter include pain along the course of ureter and muscle spasm, intermittent chills and fever, though these may not appear until some time after the operation when infection or toxic absorption from extravasated urine has had a chance to be effective. At first there may be nausea and vomiting, which usually cease after 24 hours. The patient lies in bed with the leg of the affected side drawn toward the abdomen in an attempt to relieve the contraction of the irritated iliopsoas muscle.

The early physical findings of ureteral ligation or marked angulation producing obstruction are abdominal distention and flank pain. Renal manifestations in some instances may remain in a quiescent state for months or even years before hydronephrosis, pyonephrosis, or complete atrophy of kidney develops. When the renal duct has been traumatized by needle puncture, incision, segmental resection or necrosis from application of clamps or extensive stripping, and an intraperitoneal urinary extravasation occurs causing acute peritonitis, death may result within a few days. More often, however, the urine finds its way to the surface by the formation of a ureterovaginal fistula, or drainage of urine from the abdominal wound. When both ureters are ligated, absolute anuria is present from the time of surgery.

FIG. 1. Case 1. Excretory urogram demonstrates severed left ureter and extravasation. Accident occurred during operative removal of intraligamentous cyst.

FIG. 2. Case 2. Attempted left ureteral catheterization on eleventh postoperative day. Faulty ureteral union was demonstrated by obstruction and extravasation.

When injury to a ureter is recognized at the time of surgery, it should be repaired immediately, preferably over an indwelling ureteral catheter as a splint. Occasionally, difficulty is encountered in locating the severed ends of the traumatized duct. An investigation which requires but a few minutes is the intravenous use of indigo carmine to locate the proximal portion, and the passage of a ureteral catheter to identify the distal end of the ureter.

When symptoms develop postoperatively suggesting injury to the ureter, the use of excretory urograms, cystoscopy, and the retrograde introduction of ureteral catheters will always locate the area of obstruction, and frequently the extent of damage to the renal duct.

I would like to illustrate and in this way re-emphasize the value of our diagnostic aids in patients with ureteral injury:

Case 1. R. A., a woman aged 39, had a large intraligamentous cyst removed. The day following surgery, the patient complained of abdominal pain and distention. Urinary drainage came from the abdominal wound. On the fifth postoperative day, excretory urograms disclosed a severed left ureter and extravasation (fig. 1).

Case 2. P. E., a woman aged 60; diagnosis, intraligamentous cyst of the left ovary. During the removal the left ureter was cut. The ureter was immediately repaired by end-to-end anastomosis over a No. 8 catheter. The catheter was removed 10 days later. The patient experienced severe abdominal pain and rigidity. Attempted ureteral catheterization on the eleventh postoperative day revealed faulty ureteral union and extravasation necessitating nephrectomy (fig. 2).

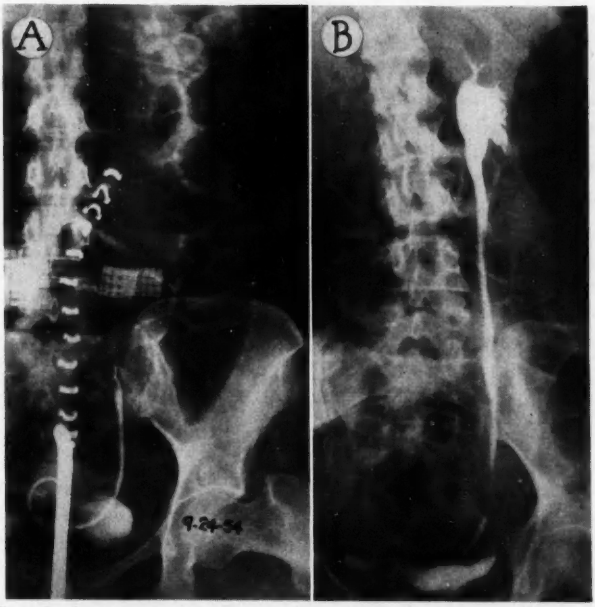

FIG. 3. Case 3. *A*, one-month postoperative retrograde urogram demonstrates normal ureter and moderate hydronephrosis. *B*, enlarged left renal shadow. Obstruction of catheter in pelvic ureter without extravasation. Opaque medium returned around catheter.

Case 3. A. L., a woman aged 40, with a diagnosis of fibroid uterus, had a subtotal hysterectomy performed. During the first 24 hours following surgery, the patient complained of severe pain in her left flank, abdominal distention, nausea and vomiting. Excretory urograms demonstrated a functionless left kidney. An attempted left ureteral catheterization disclosed an obstruction in the left pelvic ureter without extravasation. The abdomen was reopened on the third postoperative day and the ureter explored. An acute angulation of the duct was demonstrated and relieved. Apparently the condition was produced by pulling down the peritoneum to peritonealize the pelvic floor (fig. 3).

Just as surgical injuries to the ureters and bladder have increased because of the more general use of total hysterectomy, so have irradiation injuries increased because of the widespread use of radium and x-ray in the treatment of uterine malignancy, especially of the cervix. It is always advisable, before irradiation for cervical carcinoma, to perform a cystoscopic examination, including bilateral ureteral catheterization and urograms. It is only by such investigation that one can tell whether the subsequent ureteral or vesical injury is due to the operation, malignancy, or irradiation. It must be kept in mind that the most common cause of death in cervical cancer is uremia due to compression of the ureters by the malignancy.

Irradiation cystitis does not present a characteristic picture. It may be con-

fused with chronic interstitial cystitis. Usually there is a general hyperemia and at times ulceration of the bladder wall. Occasionally the ulcers are covered with encrusted urinary salts. The most common site of the lesion is in the base of the bladder near the cervix. Biopsies always should be taken of these areas to eliminate the possibility of carcinoma of the bladder. Perhaps one of the most distressing complications following irradiation of the cervix is the development of urinary fistulas. They may open directly into the vagina or may open into the cervix and thence reach the vagina. The diagnosis is established by careful bimanual palpation of the pelvis, biopsies from bladder and cervix, cystograms, and cystoscopic study.

SUMMARY

Urologists, gynecologists, and general surgeons, all assent to the belief that the incidence of bladder and ureteral injuries is higher than available data indicate. Many clinicians are averse to reporting these injuries thereby precluding accurate statistical records, although the injuries resulting from external violence are always reported when recognized.

Ureteral injuries, particularly unilateral lesions, occurring during pelvic surgery, may not be recognized or even suspected, as the kidney may silently atrophy without giving rise to symptoms. Occasionally recanalization takes place due to the recuperative powers of these organs; however, it usually results in stricture formation. Some patients may go months or even years before symptoms develop.

Trauma to the bladder or ureter, when recognized, should always be repaired at the time of surgery. When acute symptoms develop postoperatively suggesting ureteral injury, the employment of intravenous pyelograms, cystoscopy and ureteral catheterization will always aid in making the diagnosis, demonstrating the locations and often the extent of injury to the ureter.

When bladder symptoms or signs of fistula or ureteral obstruction develop after pelvic irradiation for malignant growths, the diagnosis is established by bimanual palpation of pelvis, cystoscopy, cystograms, and cervical and bladder biopsies.

THE TREATMENT OF UROLOGIC COMPLICATIONS IN GYNECOLOGY

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Injury to the ureters or bladder during performance of pelvic operations may occur in the hands of even the best surgeons. The incidence of such injuries varies from 2 per cent during performance of ordinary surgical procedures to 10 per cent during more radical operations for malignant lesions. Because of the individual variation of certain primary factors, management of injuries to the urinary tract must be highly individualized. The age and general condition of the patient, the functional capacity of both kidneys, the curability of the primary surgical lesion, and even the economic status of the patient must be weighed in conjunction with definite knowledge as to the site and type of injury.

URETERAL INJURIES

The three most common types of injury to the ureters are ligation, crushing with a hemostat, and incision or section during sharp dissection. Extensive stripping of the ureter with subsequent slough has been a less common injury. The importance of recognizing that injury has occurred before the operation is completed needs no emphasis. How often this will happen depends upon the alertness of the surgeon to its possible occurrence.

If the surgeon recognizes that he has ligated the ureter while the abdomen is still open, immediate removal of the ligature will leave little possibility for the development of fistula, but stricture may subsequently occur. In such cases, the area that has been held in the grasp of the ligature should be carefully inspected and if it is apparent that the tissue has been crushed, the area should be resected and end-to-end anastomosis performed, or the proximal end of the ureter should be implanted into the bladder, if the injury is low enough to permit this procedure.

Crushing of the ureter with a clamp usually causes enough destruction of tissue to produce permanent damage and, for this reason, the injured area should be resected and end-to-end anastomosis accomplished, or the proximal end reimplanted into the bladder.

A ureter that has been completely sectioned should be treated in the same manner. Incomplete section of the ureter may be treated by simple closure of the incised area with fine catgut sutures. It is advisable to leave an indwelling splinting catheter in place for eight to ten days, and extraperitoneal drainage should be provided in all cases.

MANAGEMENT OF LATE INJURIES

Injury to the ureter is frequently not suspected before the operation is completed. Significant diagnostic signs in the postoperative period depend upon the nature and extent of the damage. Reduced urinary excretion or complete suppression of urine may temporarily follow any extensive surgical procedure, in

which the blood pressure is significantly lowered. However, prolonged reduction of urinary output, in the absence of shock, should never be ascribed to reflex suppression. It is imperative to rule out mechanical obstruction, which can be easily accomplished by cystoscopy and retrograde catheterization. In the case of ligated ureters, occasionally the catheters may be manipulated past the ligature and advanced to the kidneys, in which case they should be left indwelling until the effects of back pressure have subsided. In any case, cystoscopy will establish the location of the injury. Intravenous urography is also of value, and there appear to be no contraindications to it. If the ureter has been severed, the function of the kidney will usually remain good and the ureter will be outlined down to the point of injury. If the ureter has been ligated, the function of the kidney will be reduced in proportion to the completeness and duration of the obstruction.

Ligatures probably should not be removed in the early postoperative period. The local tissue reaction makes this procedure both difficult and unsatisfactory. The urinary stream should be diverted by ureterostomy, pyelostomy, or nephrostomy. Nephrostomy has been the most satisfactory procedure in our experience. It can be performed by exposing the pelvis and lower pole of the kidney, without freeing or delivering the kidney from its bed. If both ureters have been obstructed, bilateral nephrostomy can be carried out in the majority of cases, without undue risk. The patient may then be allowed to convalesce in safety until the effects of back pressure upon the kidneys have completely disappeared and the tissue reaction in the area of injury has sufficiently subsided to permit performance of definitive treatment. Occasionally, the ligature will absorb and the kidney will regain its normal function. In the majority of cases, however, this fortunate circumstance will not occur. In gynecologic procedures, the obstruction is usually low enough to reimplant the proximal end of the ureter into the bladder. This will be found to be a more satisfactory solution to injuries in this area. If more than two weeks have elapsed before the injury is detected, the chances of the kidney regaining its function are diminished. Cases of normal renal function following obstruction, which had existed for a longer period, have been reported but one might suspect that in such cases the obstruction was not complete.

In patients with irreversible renal damage, the advisability of surgical intervention must be considered. If asymptomatic, hydronephrotic atrophy has occurred, the kidney may be left alone, but such kidneys if infected will require nephrectomy. In the case of ureteral fistula without irreversible renal damage, the type of possible repair will be determined by the site of injury. If there is sufficient length of ureter above the injury, reimplantation of the ureter into the bladder as near the normal site as possible is the procedure of choice. We have, on occasion, been able to reimplant the ureter through the normal orifice. That there must be absolutely no tension upon the ureter needs no emphasis. The methods by which this may be done are adequately described in the literature. Our experience indicates that equally good results can be obtained by each method, provided freedom from tension, constriction, and angulation is obtained.

The use of a sleeve or tube constructed from the vesical wall to envelop a short ureter, otherwise incapable of reimplantation, as advocated by Ockerblad and others, may be considered. Ureteral reflux, which may follow this procedure, however, will lead to progressive renal damage. If the damaged section is short and injury too high to permit reimplantation, resection of the injured portion and anastomosis are indicated. Equally good results may be obtained from each of the several methods by which this may be accomplished. With an indwelling plastic catheter used as a splint, the lower end is drawn out through the urethra by cystoscopy at the conclusion of the operation. Alternatives are the use of a splinting catheter and diversion of the urinary stream by ureterostomy above the site of anastomosis, or splinting with a T-tube. These two methods have the disadvantage of producing angulation of the ureter, and the T-tube has a tendency to produce stricture at both ends of the T. Healing should be complete by the end of two weeks. Interval evaluation, by means of intravenous urograms and cystoscopic ureteral dilatation, is required because of the tendency to formation of stricture at the site of anastomosis.

If the damage is too high to permit reimplantation into the bladder and too extensive to permit reanastomosis, the condition of the opposite kidney will largely determine the course to be followed. If the opposite kidney is normal, nephrectomy may be a wise choice. There are those who advocate ureterointestinal anastomosis in unilateral injury, but the possible immediate and late complications cannot be considered lightly. If the kidney in question is solitary or its mate diseased, one may choose ureterointestinal anastomosis, nephrostomy, or ureterocutaneous transplantation. To await spontaneous closure of fistulas is to indulge in wishful thinking at the expense of continued renal damage. On the same basis, one should never await absorption of a ligature without diverting the urinary stream by nephrostomy to protect the kidney. Even if irreversible renal damage does not result from back pressure, the local destruction of tissue produced by the ligature will result in stricture, and in some cases, permanent occlusion of the ureter. Transuretero-ureterostomy has been advocated and unquestionably there are indications for it. In the majority of cases, however, it would seem injudicious to jeopardize the opposite normal ureter in effecting union that might result in cicatricial changes in both.

The radical treatment of malignant disease in the pelvic area not infrequently involves stripping of the ureter. In such cases, the blood supply may be compromised to the extent that the ureter will subsequently slough. This usually occurs between the end of the first and third postoperative weeks. We have noticed a considerable increase in this type of injury on surgical services, where large numbers of radical procedures are performed for pelvic carcinoma. In the cases that we have seen, the ureteral damage has been too extensive to permit resection of the devitalized area with anastomosis or reimplantation into the bladder. If the injury is bilateral, and a sufficient length of viable ureter is available, ureterointestinal anastomosis may be performed. Otherwise, the choice between cutaneous ureterostomy and permanent nephrostomy must be made. There are advocates of both methods. Our experience has been that if the stump

of the ureter is brought out well beyond the cutaneous margin, there is little tendency to formation of stricture and a collecting apparatus can be worn without the aid of indwelling catheters. On the other hand, if the end of the ureter should slough and retract beneath the cutaneous margin, formation of stricture is inevitable and, in such cases, nephrostomy is preferable.

Obviously, individual problems will determine somewhat the course that may be followed. The current practice of making preoperative intravenous urograms provides information regarding the status of renal function, which is invaluable to the operator in dealing with a ureteral injury that is recognized during the operative procedure. Ligation of an injured ureter with the expectation that the kidney will undergo silent, hydronephrotic atrophy should not be considered lightly. Even with the knowledge at hand that the opposite kidney is normal, if the involved kidney harbors low-grade infection, a fulminating course may be expected to follow. We saw a recent case in which the back pressure following ligation of the ureter led to cortical infection and septicemia. The ligature also cut through the ureter, permitting extravasation of urine through the stump. Recovery followed nephrectomy and drainage of the extravasated area. Ureters, in which the lumen has become constricted in the postoperative period from scar tissue, following gynecologic operation, usually lend themselves well to reimplantation into the bladder. Ureterovaginal fistulas occur chiefly during vaginal operative procedures, and a case will rarely be encountered that will not lend itself to reimplantation. In dealing with all types of ureteral injuries, the importance of implanting the ureter into the bladder, whenever feasible, needs no emphasis. Co-operation between the surgeon and the urologist will facilitate the management of all types of ureteral injuries.

INJURIES TO THE BLADDER

Injuries to the bladder will occur during performance of both vaginal and supravaginal procedures. An incision into the bladder, recognized during the operative procedure, is treated by simple closure, followed by insertion of an indwelling urethral catheter. Leakage of urine through the wound following supravaginal procedures is usually the result of a wound in a mobile area of the bladder, and such wounds will usually close simply by indwelling urethral catheter drainage. Vesicovaginal fistulas will require plastic repair. Most of these can be successfully repaired through the vagina. An abdominal approach, with separation of the bladder from the vagina in dealing with high fistulas, and transvesical repair, in our experience have been less satisfactory. A vesicoureterovaginal fistula will occasionally be encountered. In such cases, the ureter should be cut and reimplanted into the bladder, and transvesical closure of the vesicovaginal fistula carried out at the same time or an individual problem may indicate a vaginal approach to the latter.

INJURIES FROM RADIATION

The extensive application of radiation in the management of pelvic malignancies has accounted for a considerable number of urinary tract complications.

The reported incidence is far below actual occurrences. The reactions in the bladder are of two types: first, acute reactions, which occur during therapy, are similar to those observed in the skin, and subside without treatment—and secondly, delayed reactions, which may appear one to eight or ten years later. These involve chiefly the lower posterior wall and floor of the bladder. The tissue change is that of endarteritis, which may lead to necrosis. About 75 per cent of these will eventually heal. In others, encrusted ulcers, vesicovaginal fistulas, or embarrassment to the upper urinary tract from obstruction of the intramural portions of the ureters, develop as a part of the sclerotic process. The majority of radiation ulcers will eventually heal and, in those cases, the bladder capacity may be restored to normal. In others, contracture will reduce the bladder capacity to the point that frequency amounts to total incontinence of urine. In such cases, the upper urinary tract is dilated. Vesicovaginal fistulas resulting from radiation reaction are impossible to repair because of the poor circulation to adjacent tissue. In both of these conditions, diversion of the urinary stream is indicated by ureterosigmoid anastomosis, if feasible. Otherwise, cutaneous transplant or nephrostomy should be done. Injuries to the urinary tract that result from radiation therapy emphasize the importance of evaluating the urinary tract in connection with the interval postoperative studies.

SUMMARY

The incidence of urologic injuries during gynecologic operations ranges from 2 per cent to 10 per cent. The method of handling such injuries will depend upon the site and type of injury, the age and general condition of the patient, the functional capacity of both kidneys, the curability of the primary surgical lesion, and even the economic status of the patient.

The most common ureteral injuries are ligation, crushing, section, and extensive stripping of the ureter. Recognition of such injuries during the operative procedure will, of course, minimize the possibility of permanent damage. Unfortunately, most of these injuries are not detected until later in the postoperative period. The importance of co-operation between the surgeon and the urologist in the management of all types of ureteral injuries cannot be too strongly emphasized.

Other urologic complications in gynecology include injuries to the bladder and those resulting from radiation treatment. Whatever the type of injury to the urinary tract during gynecologic procedures, the primary object in management is to preserve renal tissue whenever possible and to restore comfort and health to the patient.

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URINARY TRACT INJURIES IN OBSTETRICS AND GYNECOLOGY*

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Serious damage to the urinary tract during pelvic surgery is a critical misadventure. The exact incidence of occurrence of accidental injury to the lower urinary tract in obstetrics and gynecology is difficult to determine, but it is obvious that these injuries are all too frequent. In spite of the greatest care and skill, severance or occlusion of the ureter and fistula-formation have always occurred and probably always will. The increasing employment of the Wertheim radical abdominal panhysterectomy and total vaginal hysterectomy have popularized more daring surgery. We believe that if this trend continues, it is likely that more, rather than fewer, urinary tract injuries will occur in the future. When major injury is not recognized, death of the patient often ensues.

The technical repair of urinary defects sustained during gynecological surgery seems commonplace to the urologist, but anastomotic procedures are not well understood by the average pelvic surgeon. Successful surgery is simple surgery. Conversely, unsuccessful surgery is complicated. The repair of urinary tract injuries is frequently unnecessarily complicated.

Often more is learned from our mistakes than our successes. With this thought, then, we have considered certain of our errors and difficulties in this review of urinary tract injuries treated at the University of California Hospital during a recent 15-year period. It seems proper to: 1) note the incidence of urinary damage in pelvic surgery; 2) appraise the causes for this urologic damage; 3) suggest means for the avoidance of such accidents; 4) offer methods for the recognition of urological injuries; and 5) present certain operative procedures to be done by the obstetrician-gynecologist for the early correction of urinary tract damage. The most significant results of this study have been the stimulation of interest in pelvic anatomy, operative technique, and certain urological principles vital to the management of urinary tract injuries.

Sixty-two instances of major injury to the urethra, bladder or ureter, occurring in 49 different women, are presented table 1. These cases represent the experience of the Department of Obstetrics and Gynecology at the University of California Hospital during the 15-year period, 1938–1952, inclusive. During these years, 6,211 major surgical operations (including 458 cesarean sections) were done. One hundred thirty-seven radical Wertheim panhysterectomies are included in this number. Abdominal procedures account for approximately two-thirds of these major operations, and about one-half of the hysterectomies done in this 15-year interval were the total type. The incidence of urinary tract injury in this series is 0.83 per cent. Although 11 patients were originally operated upon elsewhere, the final management of all women was finally undertaken by members of the

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TABLE 1. *Urinary tract injuries*
U.C.H., Obs-Gyn, 1938–1952

Accidents Secondary to	Ureter	Bladder	Urethra	Total
Wertheim radical hysterectomy	20 (1)	5		25 (1)
Total hysterectomy (other)	7 (3)	3 (3)		10 (6)
Anterior colporrhaphy	3 (1)	5	1	9 (1)
Subtotal hysterectomy	2 (1)	4		6 (1)
Excision of cervical stump	2	2		4
Excision of ovarian cyst	2	1		3
Dilatation and curettage		2 (1)		2 (1)
Cesarean section		2		2
Excision of bladder tumor		1 (1)		1 (1)
Total	36 (6)	25 (5)	1	62 (11)

Of which: ( ) occurred elsewhere.

staff of the Department of Obstetrics and Gynecology and/or by consultants from Urology. Ward and private patients are included. The operators at the original surgery done at our institution where accidents involving the urinary tract occurred were certified obstetrician-gynecologists or were senior residents in training. We have eliminated all cases where urinary tract injury occurred in cystoscopy, and in general or traumatic surgery. We have not considered damage to the urethra, bladder or ureter by malignant disease, save where definitive pelvic surgery was employed for the elimination of cancer.

Out of a total of 62 injuries, there were 36 instances of damage to the ureter and 25 cases of bladder injury. There was but one accident involving the urethra.

URETERAL INJURIES

Our experience and that of others emphasizes Bland's[1] statement that, "In spite of the prevailing belief that ureteral injury is rare, I believe it to be one of the most, if not the most frequent, as well as the most serious, accident of pelvic surgery." The type of injury and the surgical procedures from which they resulted are shown in table 2.

Thirty-six ureteral injuries were recorded in 28 patients. Some of these women also sustained bladder injuries.

It was noted that marked stricture of the ureter (of sufficient degree to cause hydronephrosis) was the most common result of operative injury in gynecologic surgery. Thirteen of 36 injuries were strictures, and in 4 cases the ureter was completely occluded.

There were nine ureterovaginal and one ureterocutaneous fistulas and nine proven severed ureters in this series (fig. 1). All of the sectioned ureters were recognized at surgery. It is probable that several instances of ureteral division are included with the ureteral fistulas, although the fact that most of the fistulas did not appear until after the first week suggests other factors.

[1] Bland, P. B.: Atlantic M. J., **27**: 341, 1924.

TABLE 2. *Ureteral injuries*
U.C.H., 1938–1952

Original Surgery (32 Patients)	Ureteral Stricture	Ureteral Severance	Ureteral Fistula	Ureteral Occlusion	Total
Wertheim radical hysterectomy	8	4	7 (1)	1	20 (1)
Total hysterectomy (other)	3	1 (1)	3 (2)		7 (3)
Anterior colporrhaphy	1 (1)			2	3 (1)
Subtotal hysterectomy		1		1 (1)	2 (1)
Excision of cervical stump	1	1			2
Excision of ovarian cyst		2			2
Total	13 (1)	9 (1)	10 (3)	4 (1)	36 (6)

Of which: ( ) occurred elsewhere.

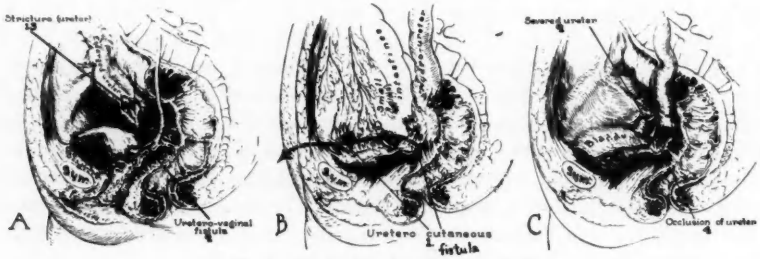

FIG. 1. Ureteral injuries sustained

The major cause or reasons for the urinary tract damage was apparent in each of the 28 cases. Admittedly, several factors probably played a role. Moreover, other reviewers may correlate certain of these causes differently. In our opinion, however, it would seem that complicated surgery, with difficult dissection, was associated with ureteral damage in 13 (46 per cent) of the patients. This represented the largest group of ureteral injuries. Faulty technique was responsible for nine (32 per cent) of the cases. Poor exposure, making dissection awkward, occurred in five (18 per cent) of the cases. Anomalous ureters were met and damaged in one case (4 per cent).

Avoidance of ureteral injury. The avoidance of urinary tract damage is, of course, more important than the methods of repair—if we believe that "an ounce of prevention is worth a pound of cure." Preoperative urological study and preparation of the patient are most important where cancer, tumor, endometriosis, or infection involve the pelvic structures. The patient presenting such lesions should be admitted to the hospital several days prior to surgery and urinary function tests obtained. These should include a phenolsulfonphthalein determination, a dilution-concentration test and excretory urography. If incompetency or distortion of the urinary tract is discovered, further studies involving cystoscopy, retrograde pyelography, and including individual kidney function tests, will be required.

Insertion of ureteral catheters preliminary to difficult pelvic surgery has generally been considered good practice. Brown[2] states, however, that it is occasionally impossible to locate the ureter by palpation even with a catheter in situ. Latzko and Schiffman[3] insist that, in most cases, preoperative ureteral catheterization is superfluous and not entirely free from danger. They believe that inlying ureteral catheters should not be employed as a routine. Current urological thinking, however, favors the insertion of adequately placed, sizable x-ray ureteral catheters before surgery. The main deterrents to preoperative catheterization seem to be: reluctance on the part of the surgeon to call a cystoscopist for consultation, the added cost, and the brief delay in effecting the necessary surgery. A catheter will facilitate ureteral repair, if this is found necessary. It will also represent an inlying splint, as well as a drain, in cases where trauma, kinking, or partial suture-obstruction to the ureter occurs. The rare occurrence of ureteral damage in our cases, which were properly prepared and where ureteral catheters were placed, attests to the value of anticipating catastrophe.

Incomplete mobilization of the bladder from the cervix in total hysterectomy, done vaginally or abdominally, invites accident by retaining the ureter too close to the field of clamps and ligatures. Adequate dissection of the bladder from the cervix may be particularly difficult when previous surgery or irradiation has been effected. Sharp dissection is often necessary, and time-consuming meticulous surgery may prevent serious bladder or ureteral injury.

It has been emphasized that one should never tie vessels of the lower uterine segment unless the peritoneum has been turned out. In a Wertheim total hysterectomy, one should leave the ureter attached to the peritoneum laterally in its upper portion and medially in its lower portion.[4] Vaginal closure by preliminary development of the pubocervical fascia, as described by Richardson[5] and also by Judd,[6] reduces the likelihood of ureteral and bladder injury.

Four danger zones have been described where injury to the ureter may occur. The *first*, but least dangerous, is the point where the ureter crosses the iliac vessels. The *second* is the ovarian fossa where the ureter comes in close proximity to the adnexa—so long as the ovary and tube remain in normal position. The *third*, and most serious point where damage is likely, is the ureteral slit where the ureter is crossed by the uterine vessels. Scarring or distortion may occur here. A *fourth* danger point is at the base of the bladder, where incisional damage or kinking of the ureter can occur. At this last point, traction extending into the interureteric ligament may obstruct the ureter—and this is particularly likely during attempts at vaginal closure of vesicovaginal fistulas.[7]

Damage to the ureter may result from reduction of its blood supply during dissection, for example, when the ureter is elevated, as in the Wertheim operation. According to Anson,[8] the ureter enters the lesser pelvis by passing over the

[2] Brown, P. J.: Am. J. Obst. & Gynec., **28:** 879, 1934.
[3] Latzko, W. and Schiffmann, J.: Halban-Seitz Biol. und Path. des Weibes, **5:** 1271, 1928.
[4] Stoeckel, W.: Veit's Handbuch der Gynakologie, Ed. 2, **2:** 576, 1902.
[5] Richardson, E. H.: Surg. Gynec. & Obst., **48:** 252, 1929.
[6] Judd, G. E.: West. J. Surg., Obst. & Gynec., **55:** 2090, 1947.
[7] Novak, J.: J. Urol. & Cutan. Rev., **48:** 321, 1944.
[8] Anson, B. J.: Atlas of Human Anatomy. Philadelphia: W. B. Saunders Co., 1950, p. 379.

point of division of the common iliac artery where it divides into the external iliac and hypogastric. Here, the ureter lies just above the hypogastric artery and receives a branch of its blood supply from this vessel via ascending and descending rami. The inferior vesical, a branch of either the uterine or the hypogastric artery, supplies the lower portion of the ureter, as do branches of the inferior hemorrhoidal artery. The superior vesical artery serves the ureterovesical juncture. In radical panhysterectomy, ligation or damage to these vessels endangers the ureter.

The peritoneum overlying the ureter, particularly in the lower portion, also supplies the ureter with small vessels. It must be recalled that the blood supply of the ureter is largely in the adventitia, so that wide stripping of the duct from the peritoneum and its bed may endanger ureteral nutrition. Careful preservation of the ureteral blood supply and avoidance of gross denudation of this structure will avoid delayed necrosis and fistula-formation.

Avoidance of ureteral damage. 1) Don't operate without adequate preliminary urinary tract studies and knowledge of the anatomy and pathology involved.

2) Catheterize and recognize the ureter initially in all difficult cases.

3) Identify all structures before clamping, incision and ligation.

4) Avoid undue traction and needless denudation of the ureter and base of the bladder.

5) Employ deft technique with fine absorbable suture material in or about the urinary tract.

6) Be careful and resourceful, and apply pressure, not mass-ligature, for hemorrhage; then, secure the bleeding point.

7) Splint the ureter, drain the bladder, and drain the wound cavity (extraperitoneally) in suspected urinary tract injury.

8) Order ample and well-chosen chemotherapy in complicated cases.

In pelvic surgery, the grave fault lies not so much in the injury of the ureter (or bladder) but in the failure to recognize this damage. The most important consideration is the provision for adequate drainage of the kidney, whether by properly executed reanastomosis or by diversion of the urinary stream. The dangers of unrecognized ureteral damage lie in extravasation of infected urine. This will finally lead to irreversible pathological changes.

After major abdominal surgery, the course of the ureter should be traced, beginning at a point well above the operative area and extending to the insertion of the ureter into the bladder. The fact that the ureter contracts actively aids in its identification. If doubt still exists as to its integrity, indigo carmine or dilute methylene blue can be injected into the proximal ureter to note extravasation or obstruction. An alternative method is to place two fine stay-sutures in the ureter and through a small incision between them, insert a 5 or 6F ureteral catheter toward the bladder. If a ureteral catheter has been placed prior to surgery, the surgeon himself should withdraw it to detect any undue "hang" suggestive of ligation.

A study of the 3 deaths in this series indicates that if prompt recognition, preferably at surgery, had been achieved in the two instances of bladder injury

TABLE 3. *Urinary tract injuries in obstetric and gynecologic surgery, University of California Hospital, 1938–1954*

Deaths

U.C.H. No.	Urinary Lesion	Secondary to	Lesion First Noted	Means of Correction	Result	Cause of G.U. Damage	Remarks
121098	Laceration, bladder, extensive	Subtotal abdominal hysteromyomectomy	At surgery	Closure	Death p.o. 11	Poor exposure. Large myoma	Catheter drainage but extravasation, infection. Pulm. embolus.
121408	Laceration, bladder	Manchester operation, 3° prolapse	p.o. 3	Inconclusive cystoscopy, p.o. 3, tidal drainage (no laparotomy)	Death p.o. 8	Faulty technique. Poor exposure. Laceration unrecognized.	Extravasation of urine. Infection, pneumonia. Death: sepsis.
123487	Occlusion ureter, lt.	Pelv. lymphadenectomy for ca. of cervix	At surgery	None possible. Hemorrhage	Death p.o. 7	Hemorrhage. Deliberate mass clamp compression	Death: Hemorrhage, ileus

(table 3), extravasation of urine, leading to infection and death, might have been avoided. Breach of the principles of adequate exposure and proper technique in the management of urological injury was basically responsible for these deaths. Laceration of a major vessel during radical surgery may require heroic measures, such as mass-ligature, but only at the hazard of the urinary tract.

Treatment. If the accident is recognized at the time of the initial operation, treatment is greatly simplified. Three basic urologic principles which may be overlooked must be observed for safety and for good results. First, adequate drainage must be provided for possible leakage of urine—whether a watertight repair can be done or not. Second, continuity of the urinary conduits should be attempted, since proper coaptation will decrease leakage and periureteritis, and allow proper peristaltic flow. Third, the area of repair should be splinted with an indwelling tube, to permit epithelialization and decrease scarring, with later contracture and obstruction.

With these basic concepts in mind, certain operative procedures, which apply to most cases, will be reviewed (table 4).

Deligation is indicated if mass ligatures have encircled the ureter, as proved by obstruction to a catheter passed from above. After deligation, one must make certain that necrosis or perforation of the ureter has not also taken place.

TABLE 4. *Treatment of ureteral injury*

1. Deligation
2. Anastomosis (first, establish drainage; then, re-establish continuity, and splint)
   a. Ureteroureteral anastomosis
   b. Ureterovesical anastomosis
   c. Ureterointestinal anastomosis
3. Decompression
   a. Tube ureterostomy
   b. Nephrostomy
4. Purposeful ligation of ureter
5. No treatment (at least, drain); nephrectomy

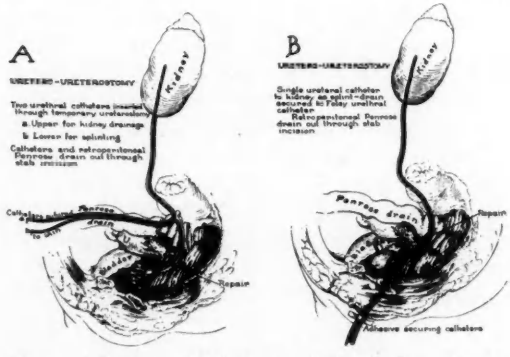

FIG. 2. *A*, ureteroureterostomy (with two catheters). *B*, ureteroureterostomy (with single catheter).

Anastomosis is most often required when the injury is detected at the operating table, since severance of the ureter is more often noticed than ligation.

Reanastomosis of the proximal ureter to the ureteral stump (ureteroureterostomy) (fig. 2) is the procedure of choice since it does not require opening of the bladder. A T-tube technique is recommended.[9] Stay sutures are placed through both cut ends, so that they can be manipulated without grasping forceps. A T-tube is notched at the T. A short incision is then made 2–4 cm. above the site for anastomosis and the lower arm of the T-tube inserted through it to traverse the anastomotic site into the distal segment. The upper arm is passed proximally. Four 4-0 chromic everting mattress sutures close the defect around the tube as a splint. It is most important to make a stab incision in the lower abdominal quadrant and dissect extraperitoneally to the site of anastomosis, so as to lead the long arm of the T-tube and a Penrose drain out of the body without traversing the peritoneal cavity.

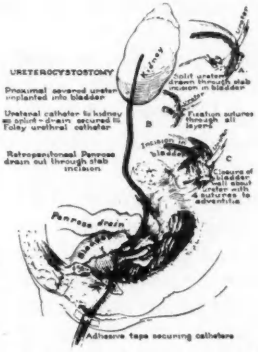

FIG. 3. Ureterocystostomy (technique)

Alternatively, if the distal stump is too short, anastomosis of the ureter to the bladder (ureterocystostomy) (fig. 3) is indicated. The bladder is adequately opened extraperitoneally, and an oblique stab incision is made in the posterior wall, close to the trigone on the damaged side. The ureter, after its end has been split (fishmouth fashion), is drawn through the bladder incision and fixed by catgut sutures which pass through all thicknesses of the bladder. Using another method, the end of the ureter may merely be cut obliquely and anastomosed, mucosa-to-mucosa, to the bladder wall. In either case, additional tacking sutures are desirable on the exterior of the bladder. This anastomosis may or may not require splinting. The best splint is a T-tube inserted through a small incision in the ureter, with the lower arm extending into the bladder and the long arm running extraperitoneally to the body wall. Another satisfactory method is the use of small *urethral* catheters through a short incision in the ureter, one running up to the kidney pelvis, and the other running down into the bladder and brought

[9] Schulte, J. W.: Discussion of article by Davis, J. P. and Wanless, H. L.: Trans. West. Sect., A.U.A., **21**: 18, 1954.

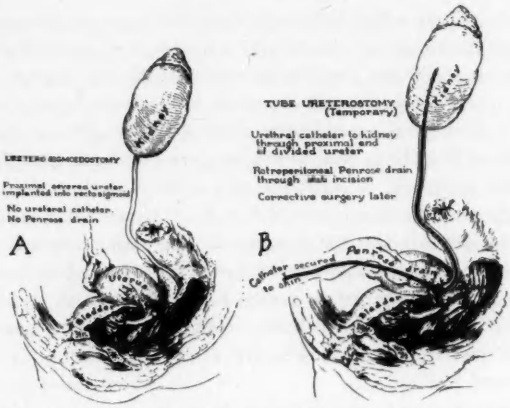

FIG. 4. *A*, ureterosigmoidostomy. *B*, tube ureterostomy

out extraperitoneally. Urethral catheters are preferable because of their flexibility and longer lumens. Or, less desirable, a ureteral catheter can be passed from the bladder to the renal pelvis, and the other end passed through the urethra and attached to a balloon catheter. In either case, extraperitoneal drainage must be provided.

If the ureter has been so badly damaged that neither of these methods is possible, the surgeon might consider anastomosis of the ureter to the large bowel (ureterosigmoidostomy) (fig. 4, *A*). The complications of this procedure (obstruction and chronic infection) so commonly follow even elective ureterocolic anastomoses, however, that we would rather recommend a simple drainage procedure such as tube ureterostomy (fig. 4, *B*). This would allow the patient to recover so that contralateral renal function can be evaluated, and a decision made between nephrectomy or the use of a segment of ileum to bridge the gap.

Decompression is indicated if there is not time for a careful, skillful anastomosis. It is greatly preferred to a poorly done implantation into the bladder or especially into the bowel. One can gain time by simply placing a small urethral catheter (10–12F) up the ureter from the cut segment and passing the butt end extraperitoneally through a stab wound in the lower abdominal quadrant.[10] The patient will recover from her operation, and the other kidney can be evaluated. Then, at some later time, with ureterograms as a guide, definitive repair can be planned. Antegrade pyelograms[11] are helpful in outlining the condition of the injured ureter.

Purposeful ligation of the ureter is not a procedure of choice for the good reason that a surgeon cannot be certain that the contralateral kidney is, and always will be, normal and free of disease. In addition, ligation is not always followed by simple hydronephrotic atrophy of the kidney. Infection may follow, or leak-

[10] Prentiss, R. J. and Mullenix, R. B.: J.A.M.A., **145:** 1244, 1951.
[11] Casey, W. C. and Goodwin, W. E.: J. Urol., **74:** 164–173, 1955.

TABLE 5. *Investigation of postoperative anuria*

age with subsequent ureterovaginal or ureterocutaneous fistula may occur. If ligation is done, however, nonabsorbable suture material is used.

If the injury is not recognized at the time of the surgery, considerable judgment is required in choosing the best time for repair and the best method for accomplishing it.

Anuria usually is caused by factors other than bilateral ureteral ligation. Table 5 is presented as a guide to differentiation. The phenolsulfonphthalein test (PSP) will distinguish real renal damage (lower nephron nephrosis or bilateral ureteral occlusion) from prerenal oliguria, caused by dehydration or even cardiac failure. A very low or absent PSP excretion after a gynecologic operation in which sutures or dissection approached the ureters is indication for prompt ureteral catheterization. If the catheters pass easily to both renal pelves and urinary flow is not obtained, renal oliguria-anuria is present. A retrograde pyelogram, using small amounts of dye, will rule out extravasation, if this is suspected.

If the catheters are blocked in the ureters, the exact site of the obstruction will be determined thereby. Dye is injected through the catheters and an x-ray film exposed, allowing estimation of the degree of obstruction.

Deligation should be attempted only if the patient is in good condition. Often, accidental ligation is found only when the patient fails to excrete urine—and by that time she is in poor general condition. In that case, nephrostomy, or even tube ureterostomy, would be preferable to deligation, because these procedures would guarantee adequate renal drainage, which the deligation would not. Also, if deligation fails, the secondary repair will be more difficult because of the added dissection.

Anastomosis is done by techniques similar to those outlined above. Nevertheless, the surgeon should not be forced by the patient to intercede too soon: many ureterovaginal fistulas heal spontaneously.

Decompression, as we have indicated, is often life-saving. A nephrostomy will make later repair easier.

Nephrectomy is desirable in older patients with damage to the kidney from infection associated with fistula. It may be required after previous failures to repair the defect. Nephrectomy should be done, of course, only after study shows the other kidney to be normal.

BLADDER INJURIES

Twenty-five bladder injuries in 25 patients are considered in the present series. We have divided the accidents into the following categories: 1) bladder incision or laceration, 2) vesicovaginal fistula, and 3) vesicoabdominal fistula, as shown in table 6 (fig. 5).

Avoidance of bladder injury. In ascribing the cause for these difficulties, it would seem that eight of the bladder incisions or lacerations were due to scarred tissues, generally the result of previous surgery and/or radiation, with complicated dissection. Five vesicovaginal fistulas are considered to be due also to difficult surgery. Four of the bladder lacerations were the result of faulty tech-

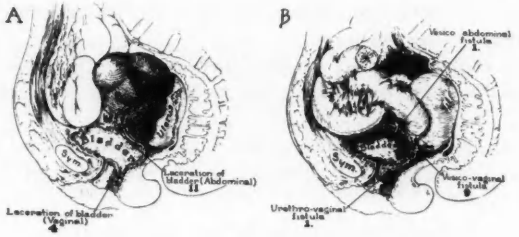

FIG. 5. Bladder and ureteral injuries

TABLE 6. *Bladder and urethral injuries*

U.C.H., 1938–1952

Original Surgery (25 Patients)	Bladder Incision or Laceration	Vesicovaginal Fistula	Vesico-abdominal Fistula	Total
Wertheim radical hysterectomy	3	2		5
Total hysterectomy (other)	1 (1)	2 (1)		2 (2)
Anterior colporrhaphy	4	1		5
Subtotal hysterectomy	3	1		4
Excision of cervical stump	1	1		2
Excision of ovarian cyst	1			1
Dilatation amd curettage		1 (1)	1 (1)	3 (2)
Cesarean section	2			2
Excision of bladder tumor		1 (1)		1 (1)
Total	15 (1)	9 (3)	1 (1)	25 (5)

Of which: ( ) occurred elsewhere.

nique, as were four instances of vesicovaginal fistula, and one vesicoabdominal fistula. Poor exposure was the principal reason for three lacerations of the bladder.

Treatment of bladder injury. The repair of bladder injuries requires their prompt recognition. The use of sterile, canned, evaporated milk, or dilute methylene blue, may serve to demonstrate a bladder defect at surgery. An indwelling catheter, without tidal drainage, for at least 10 days is proper procedure where bladder damage is noted and repaired. If a bladder fault is unrecognized and extravasation of urine occurs, cystoscopy is rarely helpful and is usually inconclusive. A cystogram is by far the best procedure to note extravasation. Occasionally, the passage of ureteral catheters may be required to differentiate the leakage from that of a ureterovaginal fistula. Secondary surgery for the closure of a damaged bladder may dispel a crisis, and perhaps a fatal termination.

In about half of our cases of bladder injury, the problem was recognized at surgery and a repair effected. Fistula formation was not uncommon, however, and leakage of urine was then recognized between the second and third postoperative weeks.

Our experience indicates that Feeney[12] is correct in stating that bladder injuries in *abdominal* surgery may occur:

1) During incision into the parietal peritoneum. (Incompletely emptied bladder. Adhesions from previous surgery. Displacement of the bladder by tumor.)

2) With downward displacement of the bladder during total hysterectomy. (Skeletonization and ligature of uterine vessels. Severance of lateral cervical attachments.)

3) At the time of dissection for removal of cervical stump, intraligamentous tumor, or in sling, "pin-up" operations for urinary stress incontinence.

4) In cesarean section, particularly extraperitoneal, when the bladder is dissected free of the anterior uterine segment.

Bladder injuries in *vaginal* surgery may occur:

1) At the division of the anterior vesical ligament and so-called pillars of the bladder.

2) In exposure of the lateral ligaments of the cervix during vaginal hysterectomy or Manchester operation.

3 During dissection for access to anterior cul-de-sac during interposition operations or vaginal hysterectomy.

4) In anterior colporrhaphy when the distal end of the posterior urethral ligament is secured to the anterior cervix.

Infection, hematoma, deep sutures, and over-distension of the bladder may be secondary causes for bladder injury and fistulas.

Two urological principles must be kept in mind when faced with a bladder injury. First, the site of repair must be adequately drained, extraperitoneally. Second, the bladder itself must be drained, so that urine cannot accumulate.

The actual closure of a fresh wound in the bladder is simple. Sufficient bladder wall is mobilized to allow closure without tension. The submucosa (preferably without the mucosa) is closed with fine catgut sutures. Nonabsorbable material is never used near the urinary tract, because it will cause a fistula to persist and may be the nidus for a stone. The muscularis and adventitia are closed in one layer with 0 chromic catgut, and then the peritoneum overlying the damaged area is approximated. A Penrose drain is inserted to the area and led out extraperitoneally.

The bladder itself is usually drained adequately by an inlying urethral catheter. If the damage is extensive, or if breakdown is possible, a cystostomy tube should be placed either vaginally or suprapubically.

Although our series is small, it would seem that laceration or incision of the bladder, if discovered at surgery and repaired properly, has an excellent likelihood of healing without complications. Vesicovaginal fistulas usually heal at secondary surgery if closed carefully three or more months after the original operation.

[12] Feeney, J. K.: Irish J. Med. Sci., p. 112, (March) 1948.

URETHRAL INJURIES

Damage to the urethra in obstetrics generally follows a long labor, with impaction of the presenting part beneath the symphysis for a protracted period of time. Traumatic vaginal delivery with laceration of the urethra by instruments or spicules of bone, as in craniotomy, may also injure the urethra. With better obstetrics, however, accidents to the urethra and bladder in parturition have become infrequent. In the series reported here, there were no obstetrical urethral injuries.

Urethrovaginal fistulas may follow anterior colporrhaphy. This lesion is prone to occur when previous surgery necessitates sharp dissection beneath the urethra, or where the surgeon boldly incises the vaginal wall for entry into the anterior vaginal cleavage planes. Although we had no such casualties, it is known that faulty repair, infection, hematoma, or inadequate closure following excision of a urethral diverticulum occasionally lead to a persistent urinary defect.

Traumatic catheterization, especially after the repair of urethrocele or relaxed vesical neck, may cause fistula-formation. The postoperative catheterization of gynecological patients with rigid catheters or stylet-guided soft catheters should be forbidden. One urethrovaginal fistula, following inept bladder catheterization by a nurse 10 days after vaginal repair, is included in our series. A glass catheter was used in this instance.

If urethral injury is recognized at surgery, it must be corrected then. Proper mobilization of tissue layers and coaptation with fine interrupted, absorbable sutures are required. Adequate provision for drainage of urine by urethral catheter or by vaginal or suprapubic cystostomy is usually necessary for successful healing. There are few indications, however, for hasty repair of urethral injuries when discovered in the postoperative period. Secondary surgery four to six months after the original operation is desirable.

SUMMARY AND CONCLUSIONS

The current trend in pelvic surgery is toward increasingly radical operations. Gynecologists should be able to avoid and to correct the numerous urinary tract injuries which become more likely during complicated or daring operative procedures.

A review of an experience of 15 years in the Department of Obstetrics and Gynecology at the University of California Hospital, San Francisco, comprising 36 ureteral, 25 bladder, and 1 urethral, injuries and their repair indicates that the radical Wertheim—as well as the traditional panhysterectomies—were associated with the largest number of ureteral accidents. Bladder damage occurred more frequently after other major surgical procedures, such as anterior colporrhaphy and subtotal hysterectomy.

Gynecological surgery involving the removal of malignant or complicated benign proliferative or irradiated lesions greatly hazard the ureter and the bladder. Inadequate incisions and poor relaxation of the patient during surgery

handicap the operator in obtaining proper exposure. Ill-advised blunt or at times sharp dissection, excessive traction and poor hemostasis are other faults in technique which encourage urinary tract injury and fistula-formation.

Urinary reparative and anastomotic procedures are not well understood by the average pelvic surgeon but are usually successful in the hands of those familiar with the proper, accepted techniques. Most frequently disregarded is provision for adequate urinary drainage from the site of repair. Careful re-establishment of continuity of the urinary conduits and the more frequent use of catheter-splints to prevent secondary complications, such as stricture-formation, are emphasized.

Practical technical details which apply currently employed urological principles for the repair of accidental injury to the urinary tract are described and illustrated.

DISCUSSION

DR. RICHARD CHUTE (Boston, Mass.): I have certainly enjoyed this valuable presentation by Drs. Rusche, Burns and Benson very much indeed. I would like to ask Dr. Burns one direct question as to what technique of reimplantation of the ureter into the bladder he uses. He has obtained excellent results.

The reason I got up here is that while I was listening to this, I had a thought about surgery in general. I realize that many of these instances of ureteral and bladder injury were in very difficult cases. They had been operated on before; they had had radiation; they had carcinoma. It is awfully easy to sit in the stands and boo the fielder who drops the fly because the afternoon sun is in his eyes. However, I am very sure that a few of these injuries happened because the operator didn't carefully identify the ureter beforehand, and that brings me to a principle that I think applies to all of us. If there is anything that you want to avoid, let us not cut along in blind fear and then have to say, "Oh, I am into it now." The thing to do, if you want to avoid the ureter, if you want to avoid the vena cava or the pleural cavity, before you do the surgery you are planning to do, whether nephrectomy, cystectomy, and so on, is to go and locate the thing you are scared of, and get it dissected free so that you know just where it is, and then you can operate more rapidly and without danger of accidents.

Before I ever did any cystectomies myself, I saw a few done by men who were considered very competent for that time. They were the bloodiest and most hair-raising operations I ever saw, and very different in technique from that shown in the fine movie of Dr. Leadbetter's which many of you saw at the AUA meeting, where the vessels were dissected out and clamped, the puboprostatic ligament was clamped, and virtually no unnecessary blood was lost. I would just like to leave you with this message which I think is terribly important in surgery in general. If there is anything which you wish to avoid and which can give you trouble, go right to it and expose it, and map it out. Then you know where your enemy is, and you can operate without any trouble from it.

We had near our tennis court in the country some very heavy, big bushes; I was trying to get a little exercise by digging out and chopping them with a pick axe, and then I said, "Oh goodness, the main water line of the tennis court goes right through here; I have got to go carefully." Then I said, Chute, don't be silly. You know where that faucet comes out. Expose the length of that pipe line, and then you will know just where it is, and you can chop away to your heart's content, and you won't hurt the line."

DR. THOMAS D. MOORE (Memphis, Tenn.): This has been a very interesting and instructive symposium concerning problems that confront all urologists from time to time. I rise chiefly to mention the subject of accidental bilateral ligation of the ureters, which occasionally occurs during difficult pelvic surgery.

These patients are anuric and are usually in a desperate condition when the urologist is called in consultation. In a review of the literature pertaining to deligation, it is noted that the mortality rate is extremely high, estimated as high as 90 per cent. Why should this be? It is because usually the surgeon goes back

and reopens the abdomen, groping about endeavoring to find where the damage has occurred, usually a time-consuming procedure.

Far less risk is incurred through the co-operation of the surgeon and a urologist, the advantage being that with a cystoscope in place when the abdomen is reopened, the cystoscopist can actually prod with a stiff ureteral catheter the one or more obstructed points in each ureter, permitting quick release of the offending sutures, and on insertion of the catheters into the renal pelves they are left inlying, thus sparing the patient the necessity of nephrostomy and a prolonged period of morbidity.

In one such case several years ago, the patient was re-examined 2 years later, and on review of the pyelograms there was no evidence whatever of the ureters having been ligated.

What is the best disposition of the ureter that has been accidentally severed and recognized immediately? Many methods of ureteral anastomosis have been described. I should like to call your attention to the experimental work on dogs that was carried out some years ago by Davalos, in which he demonstrated that eversion of the mucosa in ureteral anastomosis results in a minimal degree of scar and therefore far less likelihood of cicatricial contracture or stricture.

Some time ago one of my residents, Dr. Charles H. Harrison, had an opportunity of using this technique when he was called into an adjoining operating room because of the accidental severance of a ureter at the level of the crest of the ilium. The severed ends were converted into equilateral triangles by stay sutures and were anastomosed with 0000 chromic catgut, employing essentially the same technique as one would in anastomosing a severed artery with eversion of the intima. This patient has been observed at regular intervals since and thus far there has been no pyelographic evidence of the point where the ureter had been severed.

Dr. Rubin Flocks (Iowa City, Iowa): I want to say how much I enjoyed all the papers today. They were very excellent and very informative. There is one complication even worse than Dr. Hand just stated that emphasizes the need for preliminary pyelography, as has been stressed by several of the speakers.

This patient was seen two years ago. Cystoscopy showed that the bladder was normal; clear urine, and good function from both ureteral orifices. Catheters were not used. Pyelography was not carried out. The gynecological surgeon proceeded to do a radical removal of the pelvic organs for this patient's extensive inflammatory disease, and the organs were found to contain a pelvic kidney, which was the only kidney the patient had.

Dr. Thomas E. Gibson (San Francisco, Calif.): This very interesting symposium has been most instructive and worthwhile.

One of the most frequent complications of gynecological surgery as well as obstetrics is the occurrence of vesicovaginal fistula. A point that should be emphasized is that it is possible for a vesicovaginal fistula to heal spontaneously if prompt urethral catheter drainage is instituted. Recently, such a case came to my attention. Following hysterectomy, vaginal leakage of urine occurred through a small opening seen cystoscopically in the fundus of the bladder A Foley catheter was passed to the bladder per urethram and connected to a drainage bottle.

The catheter was removed after 2 weeks and no further leakage occurred. Suction is not necessary in such cases, but it is important that the catheter be made to drain continuously and that the drainage bottle always be kept at a lower level than the bladder even though the patient is permitted to get up and walk around.

A rare complication of anterior colporrhaphy is complete anuria due to constriction of the lower ends of the ureters by plicating sutures. In one case of this sort I was unable to catheterize the ureters. The surgeon corrected the situation by removing the offending sutures. There was prompt return of renal function and no late sequellae developed.

Dr. John K. Lattimer (New York, N. Y.): May I ask a question of Dr. Rusche in regard to the legal complications? Does he have any words of wisdom about breaking the news of a mishap to the patient, or how such matters should be handled?

Dr. Fletcher H. Colby (Boston, Mass.): It seems to me that in some instances of severe radiation reactions, some preventive measures can be taken, and I don't think the severe reaction is always due to excessive irradiation, but sometimes it is due to the fact that some patients can tolerate large doses of irradiation, whereas other patients cannot.

But when a patient who has had radiation, external radiation or radium who has a large angry lesion at the base of her bladder in the region of what was the cervix, then I think if those patients are immediately put on catheter drainage that some of these terrible vesicovaginal fistulas may be avoided, and that has been our experience. I would like to know what Dr. Benson says.

Dr. Gilbert J. Thomas (Santa Monica, Calif.): I think we should emphasize when the urologist is asked to assist the gynecologist or the general surgeon in pelvic surgery, that it isn't enough to pass ureteral catheters to orient these structures. If leaded or x-ray catheters are used, these will reveal, on the x-ray film, ureteral displacement by the tumor but anomalies may not be found or recognized. Bilateral pyeloureterograms should be made. These will reveal multiple ureters, functionless kidneys, pelvic kidney, and etc.

We believe that the urologist, the gynecologist, and the general surgeon should co-operate and lend every possible technical help and advice in conditions of this character and magnitude. This is our plan at the University of California at Los Angeles. The gynecologists are called in to help us, and vice versa. If we are going to use the ileal loop, we like to have the help of the intestinal surgeon.

At the University of California, Los Angeles, we have used the ileal loop to replace the ureter. I am going to give you just one case report out of four instances to show you why it was necessary to do this.*

This 25-year-old married Japanese woman had noted intermenstrual bleeding for approximately seven months. A diagnosis of "stage 1" carcinoma of the cervix was made, and she received 4000r, which was more than the 2500r that Dr. Benson advised for radium vaginal pack for tumor mass shrinkage.

She had normal excretory urograms prior to the radical hysterectomy which

* This technique will be reported by Drs. Vincent Moore, J. G. Moore, Robert Weber, Ed Woodward, and Willard Goodwin of our staff.

followed on July 24, 1953. At the conclusion of surgery, her gynecologist thought the left ureter might have been injured in this extensive dissection. Accordingly, catheterization of the left side only was requested. Subsequent pyelograms showed a slight narrowing of the ureter in the area of the *left pelvic brim*. "Pull out" films showed only slight *left pyelectasis*.

Because the gynecologist was quite certain the right side had not been damaged, *it was not examined by retrograde pyelogram* at this time.

The patient had much pelvic pain, probably due to ureteral catheters passed into the left ureter. Upon their removal, the discomfort lessened. Excretion urography was recommended but not performed before the patient was discharged from the hospital.

On her fifteenth postoperative day, at home, the patient had a low grade fever but was not seen again by the urologist until September 1953. At that time, she admitted having had vaginal drainage for 3 weeks. This had been continuous day and night, but she had been reluctant to reveal this to her doctor before the appointed time for her to return to the clinic at the hospital.

Examination of the vaginal vault in September revealed a dimple with suspicious ulceration on the left side which was thought to be a left ureterovaginal fistula.

Retrograde pyelograms revealed a right catheter to be coiled ("remember, we didn't think that it was necessary during the first postoperative cystoscopy") behind and outside the bladder. Aspiration withdrew about 90 cc very thick pus. Injection of contrast medium indicated a huge retrovesical abscess, which could not be definitely palpated even after films had been taken.

A 5F ureteral catheter could be passed through the left ureteral meatus without difficulty and pyeloureterogram revealed no evidence of fistula on the left side. Because of this massive retroperitoneal and retrovesical abscess, the patient eventually had a right nephrostomy.

The patient also required a left nephrostomy.

When the ureteral obstruction on that side failed to respond to catheter dilatation—at the time of her kidney drainage and by extensive flank incision, multiple Penrose drains of course had to be placed deep in both flanks after approximately 15 cc of pus and urine were removed. After the patient's nephrostomy drainage had been instituted, there was a continuous battle with stone formation, as is shown here. The patient could completely occlude both nephrostomy tubes with calcium deposits in about ten days, even with the generous use of irrigating solutions.

Frequent change of nephrostomy tubes was traumatic for the patient and also for the urologist, since there was always difficulty upon the reintroduction of these tubes.

The patient finally reached an equilibrium, we thought, and began to gain weight. On March 25, 1954, she underwent reconstruction of both ureters with a single loop of ileum. At the time of surgery, no evidence of persistent or recurrent cervical malignancy could be seen or felt. *There was complete obstruction of the right ureter as far as the ureteropelvic juncture*, as you see there. A loop of small

bowel, which was prepared in the manner previously described and which measured approximately 40 cm., was connected by mucosa-to-mucosa, approximation end-to-side, anastomosed to the ureteropelvic juncture. The proximal blind loop was closed and sutured into the right upper quadrant lateral to the renal pelvis. A number 12 splinting rubber catheter was passed down through the anastomosis and milked out through the loop of small bowel. It was fastened at the ureteroileal anastomosis with a plain gut suture. The left ureter was then dissected out with extreme difficulty from a massive bit of scar tissue. The ureter was of good caliber, with slight dilatation of its upper half. A mucosa-to-mucosa anastomosis was made to the left side with a 10 ureteral catheter of rubber, fastened in place and milked through the small bowel, as described above. The lower ileum end was then attached to the bladder by mucosa-to-mucosa sutures. Ureteral catheters were again brought out through the urethra and tied to a splinting Foley catheter. The patient made an uneventful recovery following this operation and spontaneously extruded her ureteral catheters on the ninth postoperative day.

On the next day, excretory urography with the nephrostomy tubes clamped showed bilateral function with slight pyelectasis on the right side with patent prompt drainage through both anastomoses.

Three days later nephrograms showed slight delay on emptying of her nephrostomy tubes, and they were removed at this time. The nephrostomy on the right dried up within 24 hours, but the one on the left continued to drain for approximately a week. The patient was discharged home the eighteenth postoperative day without complaint, but she wore an indwelling urethral catheter.

(Slide) The subsequent followup has been marked by the excellence of her clinical improvement, and complete freedom from complications. Her chemistry studies and excretory urograms taken on March 1955, one year after surgery, showed a persistence of slight hydronephrosis which she had had ever since her nephrostomies were done. She continued to enjoy full normal activity without any complaints. She got to the bathroom once during the night, according to instructions. She has no residual urine but continues to have, of course, mucus shreds and so forth, in the urine.

We have had four of these operations done by the younger men in urology with the assistance of the general surgeon, and by consultation with the gynecologist.

Dr. John R. Hand (Portland, Ore.): I have enjoyed this interesting symposium by Dr. Rusche, Dr. Burns and Dr. Benson. In my file of ureteral and bladder injuries following gynecologic procedures, there is one complication that wasn't discussed today. Since it represents the most severe complication I have seen, I thought I should mention it.

This patient underwent repair of a cystocele. I was asked to see her about the tenth day at which time she had uremia. On cystoscopy I was surprised to see nothing but muscle fibers throughout the bladder.

Investigating the cause, I learned that the surgeon had left 10 per cent silver nitrate solution in the bladder instead of the 1 per cent solution he had requested.

The silver salts remained impregnated in the bladder for some months. She has been comfortable the last 4 years with bilateral nephrostomies.

Dr. Benson's remark about ureteral catheterization reminds me of a story that a gynecologist told me he was in the operating room with the great Wertheim. The operation was proceeding and all at once Wertheim looked up and said: "Before this operation, I put the cathēēter into the urēēter and now I have just cut the urēēter, cathēēter and all!"

Dr. Edgar Burns (New Orleans, La.): In answer to Dr. Chute's question, I should like to say that we have had the usual complications encountered by others in the management of these problems, and our best results have been obtained in those cases in which attention was directed largely toward mobilization of the bladder and, thereby, reducing the necessity for extensive freeing of the ureter. As indicated a few moments ago, a disturbance of the blood supply to the ureter in this area may account for failure to obtain a good result. In so far as the method of putting the ureter through the bladder wall is concerned, like a great many other plastic procedures, the simpler the method, the better the results obtained. The method used in the management of the cases shown here today was simply an incision of the serosa, separation of the muscle fibers with fine-point clamp, and incision of the mucosa. The ureter was then pulled through, fish-mouthed and attached to the bladder mucosa, care being taken to avoid tension and angulation.

In so far as Dr. Moore's question is concerned, I quite agree that an attempt to deligate the ureter in the early postoperative period will be found both difficult and unsatisfactory, and so stated in the body of the paper. Of the various methods of reanastomosing the ureter, we have found the one suggested by Davalos to be very satisfactory.

The case shown by Dr. Thomas is an excellent illustration of a good result obtained in the management of a difficult problem. On the other hand, I purposely avoided any reference to the use of the ileal loop in the management of ureteral injuries, in that it must still be considered somewhat in the experimental stage. The papers presented here will become a part of reference libraries, and, in discussing treatment, I have confined my remarks to methods already evaluated. Utilization of the ileal loop may well prove to be one of the methods of choice in selected cases.

In answer to Dr. Nesbit's question, I can only speculate and speculation does not always provide the correct answer. I rather suspect, however, that the disturbed renal function in the case he cites was on a circulatory basis.

Dr. Fletcher Colby (Boston, Mass.): I am very glad you made the remarks you did. I think they should be incorporated in our transactions and I wonder if Dr. Leadbetter would also add a little to this discussion about the transplantation of certain portions of the intestinal tract of the bladder.

Would you like to say something about it?

Dr. Wyland F. Leadbetter (Boston, Mass.): I don't think there is much that I can say, except that many procedures under discussion are essentially experimental in the sense that we don't know what the long-term results are going

to be. I don't think they should be otherwise presented until we have followed them long enough to know what the ultimate results are going to be.

When I talked about the ileal loop the other day, I was talking about its application to patients who had had almost every other type of procedure that I could think of to straighten them out, and really were up against it. I think those are the type of cases where one should use these procedures. Nothing else is possible. I think what Dr. Burns had to say is very significant. We should keep it in mind, particularly the necessity of coming back and letting you and the urologists at large find out what happened to the patients and procedures we have discussed.

Dr. Ralph C. Benson (San Francisco, Calif.): I should also like to thank the discussants. With regard to deligation, I think that Dr. Burns has struck the proper note, that it is very difficult to actually find a point of ligation, certainly in abdominal cases, and this applies also to vaginal hysterectomy.

I think, however, that if it is principally a cystocele repair, particularly where there is a good deal of desensus, where a Manchester operation has been done, that it might be wise to try to deligate and then, if this is not feasible, to go further perhaps with nephrostomy.

In one case of this type we had such a problem and, believe it or not, we deligated her twice. The repair was done in two layers. We felt that we had cut the sutures and, sure enough, we did get some urine flow. Nevertheless, we realized that there was still a ureteral kink. So, the next day we did the same thing all over again in the second plane. Strangely enough, although this woman had a marked prolapse, the final result was very satisfactory, with a minimal number of sutures.

I remember an old general surgeon who never operated upon a patient but what he told her that hers was a "very complicated problem," and that it might be necessary to do the procedure in *two* stages; so that if ever he had a complication, he had told her about it.